

# Module 2

## The Cell

### Learning Objectives

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- Define cell. Roughly enumerate the large number of cells and cell types and provide some examples of how cells differ based on function.
- List the roles of membranes in cellular physiology. Describe processes by which cells compartmentalize material for exchange intracellularly and intercellularly.
- List the major organelles of the cell and state the associated function(s). Roughly enumerate the organelles per cell. Synthesize ideas regarding differential organelle number in specialized cells.
- Describe physiological events that would lead to cellular proliferation. List the steps of mitosis and cytokinesis and identify key cellular features related to the steps of proliferation.
- Describe physiological events that would lead to cellular proliferation. List the steps of mitosis and cytokinesis and identify key cellular features related to the steps of proliferation.
- Define apoptosis and necrosis and describe the cellular processes associated with each. Provide examples of where apoptosis and necrosis occur in physiology.

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# The Cell (new for CC-OLI)

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## Learning Objectives

- Define cell. Roughly enumerate the large number of cells and cell types and provide some examples of how cells differ based on function.

Cells are the basis of complex life – the basic structural unit of living things. All life is comprised of cells of one type or another.

The primary advantage of the cell is to buffer complex macromolecules from environmental variation. The cell membrane encloses the cell's interior – a water-based medium called cytoplasm. The isolation and compartmentalization of chemical reactions allows large macromolecules to interact and catalyze in highly specific ways that would be impossible in an unbuffered medium. Hundreds of types of molecules serve different roles. Scaffolding molecules structure the cell's interior. Other macromolecules are specialized for specific functions: replication, ingestion, excretion, responsiveness and cell-to-cell interaction.

Within the body, cells represent a level of organization between organelles, which in turn are comprised of specialized macromolecules, and tissues, which are collections of specialized cells. Brain, kidney, liver, muscle and lung tissues differ from each other because of the structure and function of their constituent cells. Thus, the cells comprising each tissue type vary in shape, size and interior structure to permit their specific physiological function within the tissue.

Each cell process is carried out in a specific location in the cell, often located in or around an organelle. Think of an organelle as a level of organization between macromolecules and the cell. Organelles carry out specialized tasks within the cell, localizing functions such as replication, energy production, protein synthesis, and processing of food and waste. The various tissues differ in the arrangement and number of organelles, as well as structurally, giving rise to the hundreds of cell types found in the body.

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# The Cell

To put the course in perspective, we begin by exploring the cell and the components of the cell called organelles. The focus of this course is to understand the components of the cell, how they interact with each other, how they are created, destroyed and how they regulate transport, growth and division of the cell. We will examine the controlled chemical environment a cell maintains and what restrictions this places on the types of chemical reactions it can perform. This background is vital to understanding key processes such as how a cell releases energy from glucose, makes and folds proteins, and goes through growth and cell division.

Above is a caricature of a eukaryotic cell. Many of the cell components are hyper links that will provide you with an image showing these same structures in a living cell. This illustration highlights one of the goals of the course which is to expand your view of biology by bridging from classic simple illustrations to images generated from actual data. In addition, you will develop an understanding of the fundamental processes used in this imaging method.

## Practice

This exercise uses the Cell to let you test your knowledge of the functions of the organelles.



### [The Cell Quiz](#)

# Membranes (new for CC-OLI)

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## Learning Objectives

- List the roles of membranes in cellular physiology. Describe processes by which cells compartmentalize material for exchange intracellularly and intercellularly.

The diversity of life began when membranes enclosed packets of self-replicating molecules, thus providing a protected medium buffered against environmental changes outside. Besides enclosing the cell, membranes act as guardians of the cell, permitting passage of molecules in and out.

Membranes also serve within the cell as the structural components of organelles. Membranes are typically comprised of two layers of lipid fat. Most proteins interact with membranes in some way. Within the layers, often stretching across, are embedded proteins and other macromolecules. These proteins govern much of the cell's interaction with its environment. Malfunctions in membrane proteins can have severe consequences. For example, cystic fibrosis is caused by a gene mutation that impairs functioning of a chloride ion channel protein. Membranes harbor other molecules, such as carbohydrates, which play role in immune responses.

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# Lipids

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## Learning Objectives

- Be able to define the functions of each of the classes of lipids.
- Be able to explain how the different structural features of fatty acids influence their role in phospholipids and fats.
- Be able to define the amphipathic character of a phospholipid and glycolipid.
- Be able to name and identify the ester bonds between fatty acids and glycerol and the glycerol and phosphate.
- Be able to describe and identify the difference between a liposome and a micelle.
- Be able to describe and diagram the characteristic features of the fluid mosaic membrane.

## Introduction to Lipids

The cell is composed of two distinctive environments: the hydrophilic aqueous cytoplasm and the hydrophobic lipid membranes. The lipid environment is defined by the family of molecules that are characterized by their hydrophobic nature and their common metabolic origin. Three members of the lipid family of molecules will be discussed in this course: fats (triacylglycerol), phospholipids, and steroids.

## The Structure of Lipids

Lipid molecules are slightly soluble to insoluble in water. Lipids are hydrophobic because the molecules consist of long, 16-18 carbon, hydrocarbon backbones with only a small amount of oxygen containing groups. Lipids serve many functions in organisms. They are the major components of waxes, pigments, steroid hormones, and cell membranes. Fats, steroids, and phospholipids are very important to the functioning of membranes in cells and will be the focus of this tutorial.

### Fats (triacylglycerols, triglycerides)



Fats are synthesized from two different classes of molecules: fatty acids attached to the alcohol glycerol. The fatty acids are generally, 16-22 carbons long, unbranched hydrocarbons that terminate with a single carboxyl functional group. The fatty acid can be of two types: saturated and unsaturated. Saturated fatty acids have no carbon-carbon double bonds (they are saturated with hydrogen) while the unsaturated fatty acids have one to three double bonds along the backbone carbon chain. These double bonds introduce "kinks" in the carbon chain which have important consequences on the fluid nature of lipid membranes. Unsaturated fatty acids have lower melting points than saturated fatty acids.



To construct a fat, or triacylglycerol, three fatty acid molecules are attached to the glycerol through an ester bond between the carboxyl group of the fatty acids and the three alcohol groups of a glycerol molecule. This is another example of a condensation reaction that results in formation of an ester in this case and the release of a water molecule. A fat molecule can be composed of one, two, or three different types of fatty acids each of which can be saturated or unsaturated.



An unsaturated fat has at least one unsaturated fatty acid whereas a saturated fat has none. Because the double bonds of the unsaturated fatty acids introduce kinks in the hydrocarbon backbone, unsaturated fats will not pack into a regular structure and thus remain fluid at lower temperatures. A saturated fat will pack well and be a solid at low temperatures.

Fats are mainly energy storage and insulating molecules. Per gram, fats contain twice as much energy as carbohydrates. Layers of fat also surround the vital organs of animals to cushion them, and layers of fat under the skin of animals provide insulation.

## Phospholipids



Phospholipids contain only two fatty acids attached to a glycerol head. This occurs by a condensation reaction similar to the one discussed above. The third alcohol of the glycerol forms an ester bond through reaction with phosphoric acid. This is another example of a condensation reaction between an acid and an alcohol with the release of water. As a triprotic acid (i.e it has three acidic functions on the phosphorus atom) the phosphate group attached to the glycerol has the potential to form ester links with a variety of other molecules such as carbohydrates, choline, inositol and amino acids. The phosphate group along with the glycerol group make the head of the phospholipid hydrophilic, whereas the fatty acid tail is hydrophobic. Thus phospholipids are amphipathic: a molecule with a polar end and a hydrophobic end. When phospholipids are in an aqueous solution they will self assemble into micelles or bilayers, structures that exclude water molecules from the hydrophobic tails while keeping the hydrophilic head in contact with the aqueous solution. View the animation that demonstrates the formation of micelles and bilayers.

### Head or Tail



Learn by Doing

## Head or Tail

Hint



Which end of the phospholipid is hydrophobic?

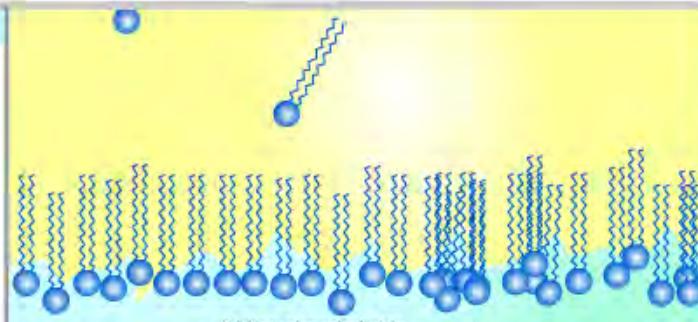
 

## Micelle and Liposome Formation

## Micelle/Liposome

Adding Phospholipids to water to form lipid bilayers and micelles and liposomes.

Micelle/Liposome



Click the green arrow to play the animation.

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*Click the green arrow to play the animation.*

Phospholipids serve a major function in the cells of all organisms: they form the phospholipid membranes that surround the cell and intracellular organelles such as the mitochondria. The cell membrane is a fluid, semi-permeable bilayer that separates the cell's contents from the environment, see animation below. The membrane is fluid at physiological temperatures and allows cells to change shape due to physical constraints or changing cellular volumes. The phospholipid membrane allows free diffusion of some small molecules such as oxygen, carbon dioxide, and small hydrocarbons, but not charged ions, polar molecules or other larger molecules such as glucose. This semi-permeable nature of the membrane allows the cell to maintain the composition of the cytoplasm independent of the external environment.

---

*A closer view of a Lipid Bilayer forming a membrane*

## Steroids

The steroids are a family of lipids based on a molecule with four fused carbon rings. This family includes many hormones and cholesterol. Cholesterol is a component of the cell membrane in animals and functions to moderate membrane fluidity because it restricts the motion of the fatty acid tails.

### Structure of Cholesterol



---

*Cholesterol in the membrane decreases the fluidity.*



Did I Get This?

## Lipid Structures

## Review of Lipids

Use the following animation to review the discussion of lipids.

# Lipid Structures

## Question 1

You find that the label on a container says it contains only hydrogenated vegetable oil. This means that during processing the number of carbon-carbon double bonds was decreased chemically. What is the result of this modification?

Select one answer.

- A. The oil remains a liquid at room temperature.
- B. The oil is now a solid at room temperature
- C. There are now more kinks in the fatty acid side chains
- D. The oil now contains phospholipid groups
- E. The triglycerides now contain fatty acids.

Check your answers

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# Lipid Structures

## Question 2

Neutral fats differ from phospholipids in that they

Select one answer.

- A. have three long hydrocarbon tails rather than two
- B. are much less polar
- C. do not make up the structure of membranes
- D. do not contain phosphorus atoms
- E. all of the above

Check your answers

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# Lipid Structures

## Question 3

Which of the following is NOT a common characteristic of all lipids?

Select one answer.

- A. They are all hydrophobic
- B. They all contain hydroxyl functional groups
- C. They are composed mainly of carbon and hydrogen atoms
- D. They are all non-polar
- E. They all do not dissolve well in water

Check your answers

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# Lipid Structures

## Question 4

All lipids

Select one answer.

- A. are polar
- B. are more soluble in non-polar solvents than in water
- C. are polymers
- D. are triglycerides
- E. are hydrophobic

Check your answers

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# Lipid Structures

## Question 5

Phospholipids are all of the following except

Select one answer.

- A. hydrolysis yields glycerol, 2 fatty acids and phosphate
- B. are the basic building blocks of membranes
- C. form rigid, permeable barriers
- D. are amphipathic

Check your answers

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# Lipid Structures

## Question 6

Acyl glycerols are characterized by all of the following except

Select one answer.

- A. contain glycerol and three fatty acids as building blocks
- B. are the storage form of fatty acids
- C. are formed by condensation of hydroxyl groups with carboxyl groups
- D. are found only as liquids.

Check your answers

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# Lipid Structures

## Question 7

Fatty Acids are all of the following EXCEPT

Select one answer.

- A. Amphipathic
- B. Contain a long hydrocarbon chain
- C. Contain a single carboxyl group
- D. Are soluble in water
- E. Can contain double bonds

Check your answers

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# Lipid Structures

## Question 8

Which of the following is not a lipid?

Select one answer.

- A. Steroid
- B. Fat
- C. Triacylglyceride
- D. plant cell wall
- E. Carotenoid

Check your answers

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# Lipid Structures

## Question 9

Which of the following best summarizes the relationship between condensation reaction and hydrolysis?

Select one answer.

- A. A condensation reaction assembles polymers and hydrolysis breaks them down.
- B. Hydrolysis occurs during the day and condensation reactions happen at night.
- C. Condensation reactions can only occur after hydrolysis.
- D. Hydrolysis creates monomers and condensation reactions destroy them.
- E. Condensation reactions occur in plants and hydrolysis happens in animals.

Check your answers

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# Lipid Structures

## Question 10

What is a triacylglycerol?

Select one answer.

- A. A protein with tertiary structure.
- B. A lipid made of three fatty acids and glycerol.
- C. A kind of lipid that makes up much of the plasma membrane.
- D. A molecule formed from three alcohols.
- E. A carbohydrate with three sugars.

Check your answers

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# Lipid Structures

## Question 11

Which of the following is TRUE concerning saturated fatty acids?

Select one answer.

- A. They have double bonds between the carbon atoms of the fatty acids.
- B. They have a higher ratio of hydrogen to carbon than unsaturated fatty acids.
- C. They are usually liquid at room temperature.
- D. They are only produced in plants.

Check your answers

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# Review of Lipids

Use the following animation to review the discussion of lipids.

## Phase Transition

## Phase Transition

Phospholipids bilayers undergo a cooperative phase transition or melting that is similar to protein denaturation. The high degree of cooperativity is due to extensive interactions between the non-polar acyl chains in the center of the bilayer. The overall structure of the lipid bilayer is not changed by this transition. However, the disorder of the non-polar hydrocarbon chains increases dramatically after melting.

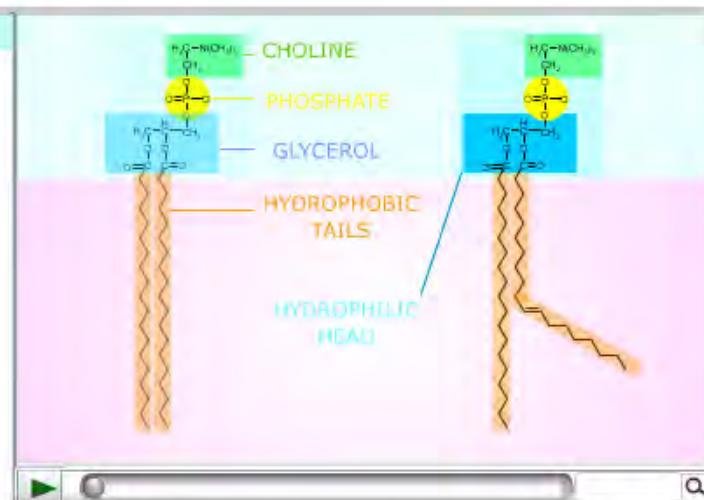
### Phase Transition

Saturated

Unsaturated

Cholesterol + Saturated

37 Celsius



Use the play/pause button on the left to start or stop the animation. Use menu to move between scenes.

# Review of Lipids

Use the following animation to review the discussion of lipids.

## Phase Transition

## Saturated

At low temperatures the saturated acyl chains are able to pack close to each other as extended chains. This is very stable configuration because of the favorable van der Waals interactions between the chains. This causes the membrane to be solid-like below the melting temperature. As the temperature rises, clusters of phospholipids melt, followed by melting of the entire bilayer. At temperatures above the melting temperature the acyl-chains are disorder or fluid.

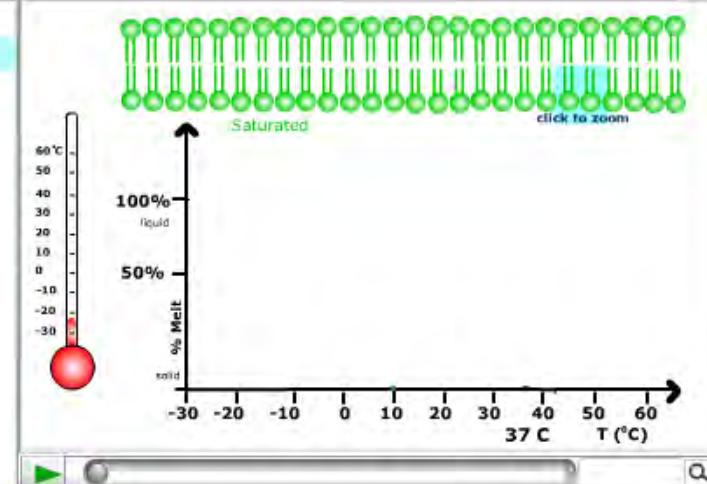
### Phase Transition

Saturated

Unsaturated

Cholesterol + Saturated

37 Celsius



Use the play/pause button on the left to start or stop the animation. Use menu to move between scenes.

# Review of Lipids

Use the following animation to review the discussion of lipids.

## Phase Transition

## Unsaturated

In an unsaturated bilayer the acyl chains have cis-double bonds that cause a sharp bend in the acyl chain. This impairs the packing of the acyl chains, reducing the van der Waals force between the chains.

Consequently, the melting temperature of unsaturated bilayers is lower than that of a saturated bilayer. In addition, the transition occurs over a broader temperature range.

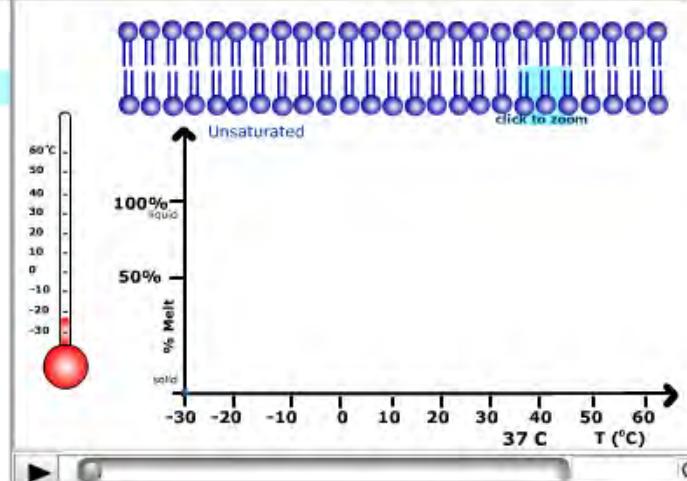
### Phase Transition

Saturated

Unsaturated

Cholesterol + Saturated

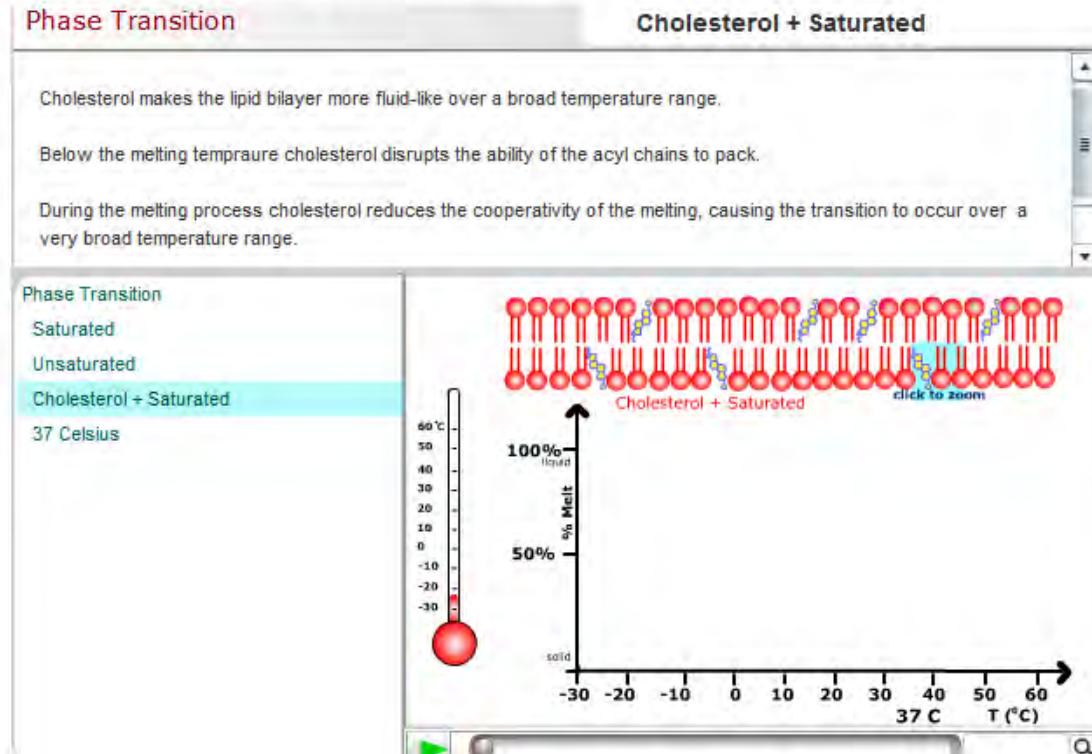
37 Celsius



Use the play/pause button on the left to start or stop the animation. Use menu to move between scenes.

# Review of Lipids

Use the following animation to review the discussion of lipids.



Use the play/pause button on the left to start or stop the animation. Use menu to move between scenes.

# Review of Lipids

Use the following animation to review the discussion of lipids.

Phase Transition

37 Celsius

This chart demonstrates the relationships of the various lipid bilayer components at 37° Celsius

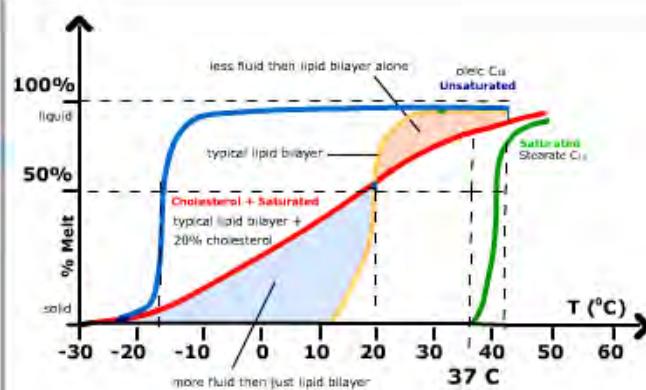
Phase Transition

Saturated

Unsaturated

Cholesterol + Saturated

37 Celsius



Use the play/pause button on the left to start or stop the animation. Use menu to move between scenes.



# Fluid Mosaic Model

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## Learning Objectives

- Be able to define the functions of each of the classes of lipids.
- Be able to explain how the different structural features of fatty acids influence their role in phospholipids and fats.
- Be able to define the amphipathic character of a phospholipid and glycolipid.
- Be able to name and identify the ester bonds between fatty acids and glycerol and the glycerol and phosphate.
- Be able to describe and identify the difference between a vesicle and a micelle.
- Be able to describe and diagram the characteristic features of the fluid mosaic membrane.

## The Structures of the Cell Membrane

### Fluid Quality of Membranes

The cell membrane must be a dynamic structure if the cell is to grow and respond to environmental changes. To keep the membrane fluid at physiological temperatures the cell alters the composition of the phospholipids. The right ratio of saturated to unsaturated fatty acids keeps the membrane fluid at any temperature conducive to life. For example winter wheat responds to decreasing temperatures by increasing the amount of unsaturated fatty acids in cell membranes. In animal cells cholesterol helps to prevent the packing of fatty acid tails and thus lowers the requirement of unsaturated fatty acids. This helps maintain the fluid nature of the cell membrane without it becoming too liquid at body temperature. The fluidity of the membrane is demonstrated in the following animation. The lipids in the membrane are in random bulk flow moving about 22 μm (micrometers) per second. Phospholipids freely move in the same layer of the membrane and rarely flip to the other layer. Flipping of phospholipids from one layer to the other rarely occurs because flipping requires the hydrophilic head to pass through the hydrophobic region of the bilayer.

---

*Click the green arrow to play the animation.*

## The Mosaic Quality of Membranes

### Proteins

Because the cell membrane is only semipermeable, the cell needs a way to communicate with other cells and exchange nutrients with the extracellular space. These roles are primarily filled by proteins. Membrane proteins are classified into two major categories, integral proteins and peripheral proteins. Integral membrane proteins are those proteins that are embedded in the lipid bilayer and are generally characterized by their solubility in non-polar, hydrophobic solvents. Transmembrane proteins are examples of integral proteins with hydrophobic regions that completely span the hydrophobic interior of the membrane. The parts of the protein exposed to the interior and exterior of the cell are hydrophilic. Integral proteins can serve as pores that selectively allow ions or nutrients into the cell. They also transmit signals into and out of the cell. Unlike integral proteins that span the membrane, peripheral proteins reside on only one side of the membrane and are often attached to integral proteins. Some peripheral proteins serve as anchor points for the cytoskeleton or extracellular fibers. Proteins are much larger than lipids and move more slowly. Some move in seemingly directed manner while others drift.

### Carbohydrates

The extracellular surface of the cell membrane is decorated with carbohydrate groups

attached to lipids and proteins. Carbohydrates are added to lipids and proteins by a process called glycosylation, and are called glycolipids or glycoproteins. These short carbohydrates, or oligosaccharides, are usually chains of 15 or fewer sugar molecules. Oligosaccharides give a cell identity (i.e., distinguishing self from non-self) and are the distinguishing factor in human blood types and transplant rejection.

## Membranes are Asymmetric

As discussed above and seen in the picture, the cell membrane is asymmetric. The extracellular face of the membrane is in contact with the extracellular matrix. The extracellular side of the membrane contains oligosaccharides that distinguish the cell as self. It also contains the end of integral proteins that interact with signals from other cells and sense the extracellular environment. The inner membrane is in contact with the contents of the cell. This side of the membrane anchors to the cytoskeleton and contains the end of integral proteins that relay signals received on the external side.

---

## Summary: Membranes as Mosaics of Structure and Function

The biological membrane is a collage of many different proteins embedded in the fluid matrix of the lipid bilayer. The lipid bilayer is the main fabric of the membrane, and its structure creates a semi-permeable membrane. The hydrophobic core impedes the diffusion of hydrophilic structures, such as ions and polar molecules but allows hydrophobic molecules, which can dissolve in the membrane, to cross it with ease. Proteins determine most of the membrane's specific functions. The plasma membrane and the membranes of the various organelles each have unique collections of proteins. For example, to date more than 50 kinds of proteins have been found in the plasma membrane of red blood cells.

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Did I Get This?

### membrane structure



My Response

### About Lipids and Membranes

## Graded Quiz



## Lipids and Membranes

Quiz

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Membrane Transport Introduction



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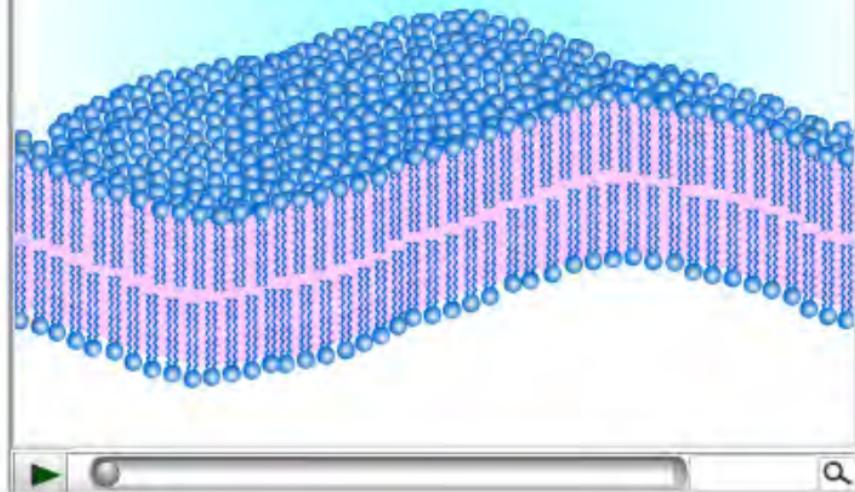
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The lipids in the membrane are in random bulk flow moving about 22  $\mu\text{m}$  (micrometers) per second. Phospholipids freely move in the same layer of the membrane and rarely flip to the other layer. Flipping of phospholipids from one layer to the other rarely occurs because flipping requires the hydrophilic head to pass through the hydrophobic region of the bilayer.

### Fluid Quality of Membranes

Membranes are not static sheets of molecules locked rigidly in place.



Click the green arrow to play the animation.

# membrane structure

## Question 1

Which of the following molecules would be easiest to extract from a membrane using aqueous solutions?

Select one answer.

- A. Integral membrane proteins
- B. Peripheral membrane proteins
- C. phospholipids
- D. glycolipids

## Question 2

Which of the following types of molecules have not been found to be associated with the cell membrane?

Select one answer.

- A. carbohydrates
- B. phospholipids
- C. proteins
- D. cholesterol
- E. All of the above are associated with the membrane.

## Question 3

Which of the following characteristics of phospholipids is responsible for the ability to form membranes?

Select one answer.

- A. They dissolve well in water.
- B. They contain saturated fatty acids.
- C. The phospholipid tails can readily form hydrogen bonds.
- D. They are amphipathic.
- E. All of the above

## Question 4

Which type of lipid is most important in biological membranes?

Select one answer.

- A. fats
- B. wax
- C. phospholipids
- D. oils
- E. triglycerides

## Question 5

Membranes are described in all of the following ways except

Select one answer.

- A. will allow transport of ions
- B. lipid bilayer
- C. uniform in thickness
- D. are fluid structures dependent on composition
- E. semipermeable barriers

Check your answers

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Close

# About Lipids and Membranes

Think of two questions about this lesson. These can be for clarification of the material or further insight. Your questions may also shape the discussions in class.

My Question 1 \*

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My Question 2

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# Lipids and Membranes

## Question 1

According to the fluid mosaic model of membranes, membranes consist of

- A. a lipid-protein sandwich
- B. a fluid phospholipid bilayer in which proteins are embedded
- C. a fluid phospholipid bilayer in which carbohydrates are embedded
- D. mainly phospholipids with scattered nucleic acids

Select one answer.

*10 points*

## Question 2

Fatty acids are added to glycerol by condensation to form what kind of bond?

- A. anhydride
- B. amide
- C. ester
- D. acetal
- E. hemiacetal

Select one answer.

*10 points*

## Question 3

Organisms that live in colder climates are more likely to have polyunsaturated fatty acids in their phospholipids.

Select one answer.

*10 points*

- A. True
- B. False

## Question 4

What is this structure?

- A. saturated fatty acid
- B. unsaturated fatty acid

Select one answer.

*10 points*

- C. cholesterol
- D. acylglycerol
- E. phospholipid

## Question 5

What is this structure?



Select one answer.

10 points

- A. saturated fatty acid
- B. unsaturated fatty acid
- C. cholesterol
- D. acylglycerol
- E. phospholipid

## Question 6

What is this structure?



Select one answer.

10 points

- A. saturated fatty acid
- B. unsaturated fatty acid
- C. cholesterol
- D. acylglycerol
- E. phospholipid

## Question 7

What is the name of this structure?



Select one answer.

10 points

- A. saturated fatty acid
- B. unsaturated fatty acid
- C. cholesterol
- D. acylglycerol
- E. phospholipid

## Question 8

Phospholipids dropped on the surface of water will

- A. spontaneously orient with the hydrocarbons oriented toward the air
- B. dissolve in water
- C. spontaneously orient with the hydrocarbons facing the water
- D. randomly orient across the surface of the water

Select one answer.

10 points

## Question 9

All of the following are lipids **EXCEPT**

- A. acylglycerols
- B. pigments
- C. phospholipids
- D. glycoproteins
- E. cholesterol

Select one answer.

10 points

## Question 10

All of the following contribute to the fluidity of the membrane **EXCEPT**

- A. high cholesterol
- B. high saturated fatty acid content
- C. presence of integral membrane proteins
- D. the interlocking of the fatty acid chains in the bilayer

Select one answer.

10 points

^ Top ^

[Save](#)

[Submit and finish](#)

# Membrane Transport Introduction

## Membrane Transport

The cell membrane provides a semi-permeable barrier between the inside and the outside of the cell. This barrier provides control for transport of nutrients, ions and signals between the highly variable outside environment and the relatively well-defined interior of the cell. This unit of the course will explore the ways in which molecules can pass across the membrane (diffusion and active transport), can be transported into the cell without passing across the membrane (endocytosis), and can send signals for actions within the cell without actually passing across the membrane themselves (signal transduction).

[^ Top ^](#)[!\[\]\(ec2ce9959d7a9398d7087608d3eaf0cb\_img.jpg\) Passive/Simple Diffusion !\[\]\(b69be60c5b3ed19eda1b528a2446c37c\_img.jpg\)](#)

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[!\[\]\(284d644ea76e79d66bb99cf994686b0c\_img.jpg\) Course Outline](#)[!\[\]\(ae13344024c8279348c5694e64c4d3df\_img.jpg\) My Scores](#)[!\[\]\(5bacabf5f9c3e31517c3cad47e00d8c9\_img.jpg\) Test My System](#)[!\[\]\(59ca1cf90991b13ee03c724de9f65da2\_img.jpg\) Email Tech Support](#)[!\[\]\(3c17afb3b4e2a3711c74398ab4c986e0\_img.jpg\) Search FAQs](#)[!\[\]\(fc56421a9367c303f1a1db2dc33bf1e8\_img.jpg\) Email Fisher](#)

# Passive/Simple Diffusion

[Hide](#)

## Learning Objectives

- Be able to describe the spontaneous direction of the movement of molecules
- Be able to describe the factors that affect simple diffusion

## Passive/Simple Diffusion:

Both large and small molecules follow the same general principle of diffusion. Molecules spontaneously move from areas of high concentration to areas of low concentration following Brownian motion. The classic example is the diffusion of a drop of ink placed in a beaker of water. The concentrated drop of color slowly disperses (diffuses) until at some point equilibrium is reached in which the beaker appears to have a uniform color. The following animation depicts this simple diffusion process. Add ink to each beaker and watch the diffusion process. After a period of time, is there a difference in the distribution of ink in each beaker? Follow the yellow ink molecule in each beaker for some time. In which simulation does the yellow ball take longer to transverse the beaker?

### Simple Diffusion

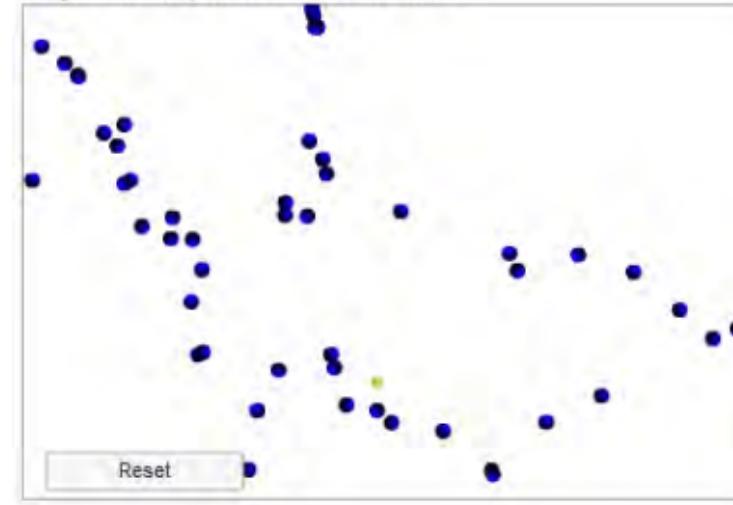
FIGURE

[Simple Diffusion, Without Brownian Motion](#)[Simple Diffusion, Brownian Motion](#)

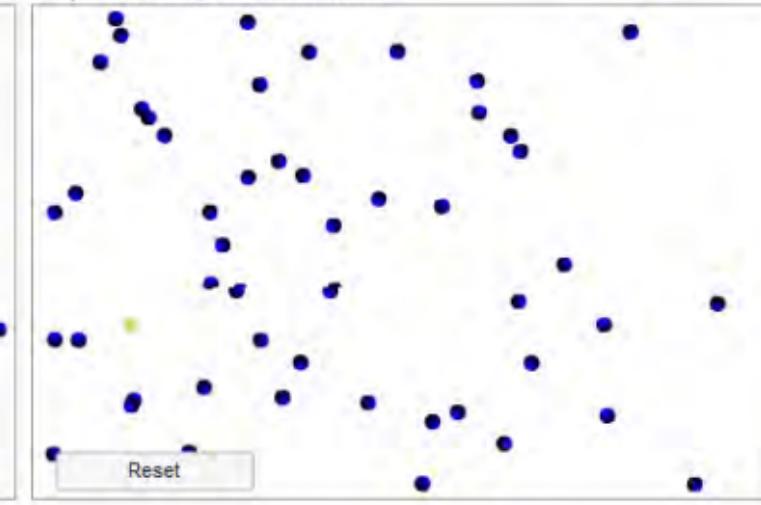
The introduction of a cell or liposome into the solution places a barrier to the molecules. As three different molecules diffuse to equilibrium they encounter the lipid bilayer depicted by the horizontal membrane across the center of the stage in the following animation. Note that one type of molecule passes freely through the lipid bilayer while the second type of molecule only occasionally passes through the membrane and the lipid bilayer is totally impermeable to the third type of molecule.

### Simulation of Three Molecules of Different Permeability

Simple Diffusion, Without Brownian Motion



Simple Diffusion, Brownian Motion



### Simulation of Three Molecules of Different Permeability



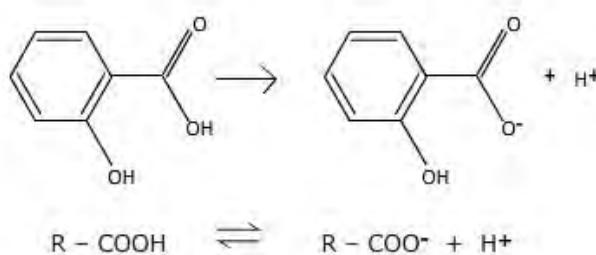
Of the first two types of molecules, the first type might include a molecule such as cholesterol which has some solubility in water but is highly soluble in the non-polar environment of the lipid bilayer and thus will freely pass into the hydrophobic environment of the membrane, distribute freely in the membrane and then some fraction will dissolve in the aqueous environment of the cytoplasm. A second example of this type of permeable molecule is water which while polar is small and able to freely pass across the membrane. The lipid bilayer is much less permeable to the second type of molecule indicating a more polar character and a larger size. Examples of such molecules are the sodium and chloride ions. As a general rule, charged molecules are much less permeable to the lipid bilayer. The third type of molecule is very polar, in many cases charged, and usually a larger molecule. Examples are carbohydrates and amino acids.

### Diffusion of Aspirin



Did I Get This?

Aspirin



In Protonated and non-Protonated States

[^ Top ^](#)
[◀](#) [Osmosis](#) [▶](#)
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usually a larger molecule. Examples are carbohydrates and amino acids.

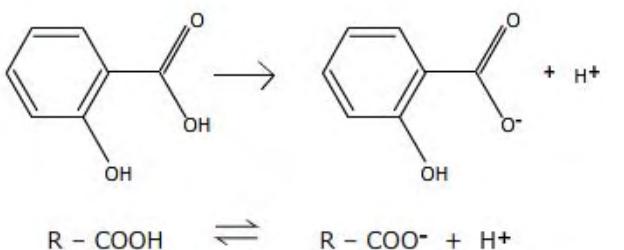


### Diffusion of Aspirin

Aspirin, depicted below, is a monocarboxylic acid with a pKa of approximately 4. Why is this molecule absorbed through the membranes of the stomach cells much more readily than through the membranes of the mouth and esophagus?

**Submit and Compare**

Aspirin



*In Protonated and non-Protonated States*

# Osmosis

[Hide](#)

## Learning Objectives

- Be able to describe the solute differences between isotonic, hypertonic and hypotonic solutions.
- Be able to describe the affect of an isotonic, hypertonic and hypotonic solution on the shape of a cell.
- Be able to describe how osmotic pressure is generated and what conditions are necessary to create high osmotic pressure in a cell.
- Be able to explain why the description of osmosis emphasizes the solvent changes

## Osmosis

Cells continually encounter changes in their external ionic environment and will spontaneously respond by attempting to equalize the concentration of ions on the inside and outside of the cell. Because the plasma membrane (lipid bilayer) is significantly less permeable to ions than water, the establishment of an equal concentration of the ions on either side of the membrane is accomplished by the net movement of water toward the higher concentration of ions to reduce the concentration. This movement of water in response to an imbalance of solute (ion) is referred to as osmosis. This is illustrated in the following simulation.



Learn by Doing

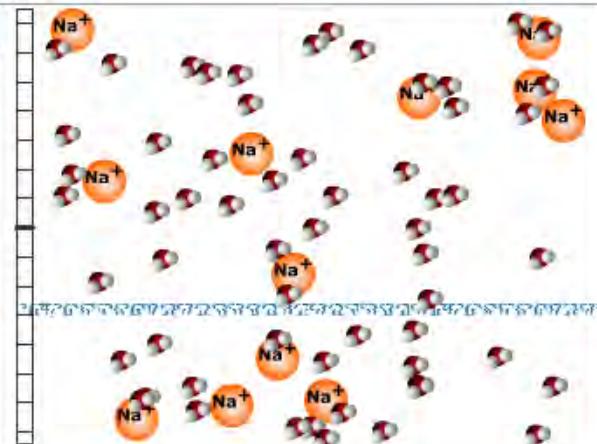


## Osmosis - direction of pressure



Learn by Doing

The system tries to equalize the pressure.



$$\frac{\text{Top}}{\text{Bottom}} \frac{[\text{Na}^+] 8}{[\text{H}_2\text{O}] 39} \approx \frac{[\text{Na}^+] 4}{[\text{H}_2\text{O}] 21}$$

$$\frac{\text{Top}}{\text{Bottom}} \frac{[\text{H}_2\text{O}] 39}{\text{Volume} 90200} \approx \frac{[\text{H}_2\text{O}] 21}{\text{Volume} 45100}$$

Done



Did I Get This?

### Osmosis - direction of pressure

Consider the constraints of a fixed membrane across the box. Once the system has reached equilibrium, on which side of the membrane is pressure exerted? What is applying the pressure?

Submit and Compare



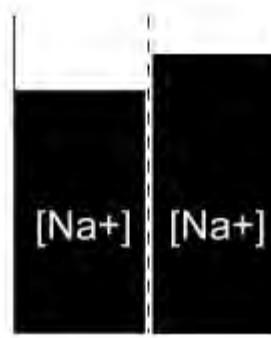
Did I Get This?

Three different conditions may exist in the relationship between the solute (ion) concentration and solvent (water) concentration across a membrane. Isotonic, hypertonic and hypotonic refer to the relative concentration of the solute (small molecules) in the extracellular (outside) space surrounding the cell relative to the solute concentration inside the cell. In an **isotonic solution**, the concentration of the solute and therefore solvent water (water potential) is the same on both sides. A **hypotonic solution** is one whose solute concentration is lower (water concentration is higher [i.e. high water potential]) in the extracellular space than inside the cell. Because the water (the solvent) can more easily pass through the membrane than can the solute (ions), the net flow is spontaneous in the direction of the solvent (water) moving from its higher concentration (high water potential) outside the cell to the inside of the cell. Conversely, a **hypertonic solution** refers to an extracellular solution with a higher solute concentration (lower water concentration [i.e. low water potential]) outside the cell than inside the cell. In this case, the more permeable solvent, water, would flow spontaneously out of the cell toward the low water potential to dilute the solute molecules and create an equal concentration of solute molecules on both sides of the membrane.



Did I Get This?

## Osmosis



## Osmotic Pressure

If in the illustration above a cap were placed on the right side of the beaker initially, the cap would

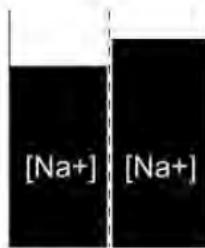


Did I Get This?

### Osmosis

In the illustration below, which side of the beaker initially had the higher concentration of solute molecules separated by the vertical membrane? How are the concentrations of solute on either side of the membrane related once the beaker has established its equilibrium?

**Submit and Compare**



experience a pressure to move up as the water molecules moved from the left to the right. The pressure necessary to prevent the cap from rising on the right is defined as the osmotic pressure. The pressure ( $P$ ) is proportional to the solute concentration on the hypertonic side of the membrane. In the example above, the solute concentration  $[Na^+]$  on the right must have been initially higher causing a net flow of solvent (water) from the left to the right. The pressure exerted on the right side, if no expansion were allowed in an attempt to attain equilibrium, is the osmotic pressure.



## Simple Diffusion Osmosis

Did I Get This?

Before leaving this page, provide the following response to the learning objectives for this topic.



## Osmosis

My Response

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Facilitated Diffusion

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# SimpleDiffusionOsmosis

## Question 1

Osmotic pressure maintains the turgor of plants because the cytoplasm of the plant cell is \_\_\_\_\_ relative to the water fed to the plants.

Select one answer.

- A. hypertonic
- B. isotonic
- C. hypotonic

## Question 2

osmosis is the movement of

Select one answer.

- A. solvent
- B. solute

## Question 3

To prevent the net movement of water from either going into or out of the cell, the solution outside the cell must be

Select one answer.

- A. hypertonic
- B. isotonic
- C. hypotonic

## Question 4

A cell is placed in pure water. The water is \_\_\_\_\_ relative to the inside of the cell.

Select one answer.

- A. hypertonic
- B. isotonic
- C. hypotonic

## Question 5

Of the following molecules, which is most likely to be not permeable to the biological membrane?

Select one answer.

- A. cholesterol
- B. water
- C. potassium ion
- D. fatty acid

## Question 6

Simple diffusion through a lipid bilayer is dependent upon the solubility of the molecule in hydrocarbons

Select one answer.

- A. True
- B. False

## Question 7

The rate limiting process for enzyme catalyzed reactions is the time it takes for the substrate to get to the enzyme in the cell because

Select one answer.

- A. substrates are too large to move fast
- B. molecules move randomly by Brownian motion rather than in straight lines
- C. the cytoplasm is an ideal solution facilitating transport of small molecules

## Question 8

At equilibrium, molecules take the shortest path from one side of the cell to the other.

Select one answer.

- A. True
- B. False

## Question 9

Molecules spontaneously move from \_\_\_\_\_ concentration to \_\_\_\_\_ concentration.

Select one answer.

- A. high; low
- B. low; high

Check your answers

^ Top ^

Close

# Osmosis

Before leaving this topic, evaluate your ability to perform each of the following tasks.

Selecting 1 means "I could do this not at all", selecting 3 means "I could do this while relying on the course material" and selecting 5 means "I could do this perfectly on an exam."

	Not At All		With Support		On My Own
I can describe the solute differences between isotonic, hypertonic and hypotonic solutions. *					
I can describe the affect of an isotonic, hypertonic and hypotonic solution on the shape of a cell. *					
I can describe how osmotic pressure is generated and what conditions are necessary to create high osmotic pressure in a cell. *					
I can explain why the description of osmosis emphasizes the solvent changes. *					
	1	2	3	4	5

^ Top ^

# Facilitated Diffusion

[Hide](#)

## Learning Objectives

- Be able to distinguish between simple diffusion and facilitated diffusion
- Be able to describe the structural and chemical characteristics of a typical 'facilitator'.

### Facilitated Diffusion

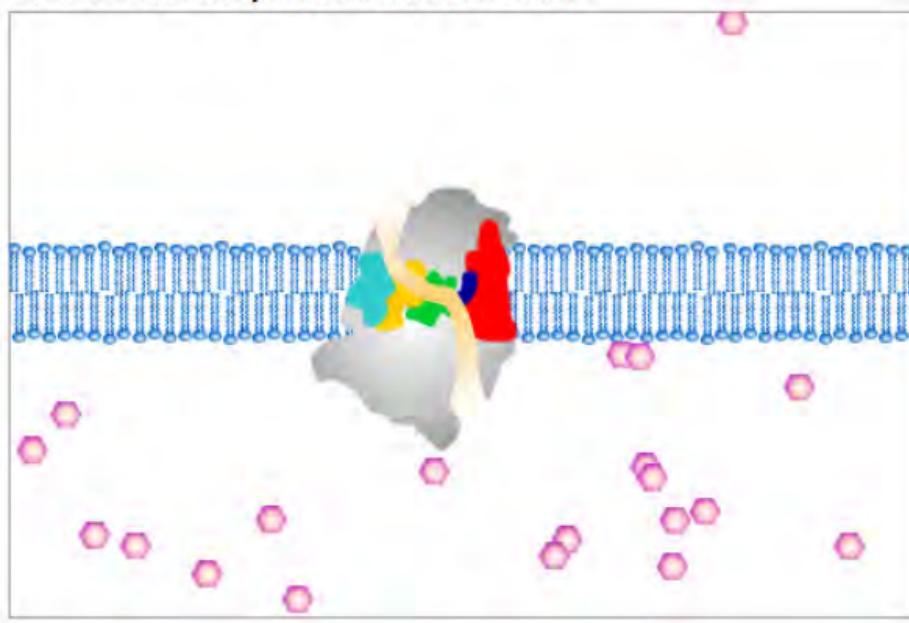
Cells must be able to move polar molecules such as nutrients and ions across the lipid bilayer of the membrane in order to carry out life processes. But the molecules will still move spontaneously down a concentration from high to low concentration. To allow the polar molecules, which are not soluble in the lipid bilayer, to pass across the hydrophobic barrier it is necessary to provide ports, channels or holes through the membrane. These channels can either allow the molecules to move freely according to their concentration differences or they can be gated channels that control the movement of the polar molecules according to the needs of the cell. In most cases these channels are very discriminatory and will only allow specific molecules to pass; another example of bioselectivity. The channels facilitate the movement of molecules that otherwise would not be spontaneously permeable to the lipid bilayer. The process of moving impermeable molecules across a membrane using channels or pores is referred to as **facilitated diffusion**. Because the molecules are moving down a concentration gradient the process is driven by simple diffusion. The following simulation depicts the facilitated diffusion of glucose across the membrane using the glucose permease transporter.

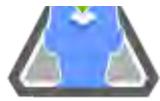
### Simulation of Simple Facilitated Diffusion



## Facilitated Diffusion

### Simulation of Simple Facilitated Diffusion





Did I Get This?



## Facilitated Diffusion with glucose permease transporter

Did I Get This?

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Active Transport

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### Facilitated Diffusion

What do you notice about the state of the system when the system has come to equilibrium? If the number of glucose molecules above the membrane is initially 100 and there is no glucose below the membrane, how many glucose molecules will be below the membrane when the system comes to equilibrium?

  
**Submit and Compare**

### Facilitated Diffusion with glucose permease transporter

The glucose permease transporter illustrated in the simulation can allow the glucose molecules to either move in both directions or it can be unidirectional from outside to inside only.

What will happen to the cell that has unidirectional transport of glucose to the inside of the cell?

  
**Submit and Compare**

# Active Transport

[Hide](#)

## Learning Objectives

- Be able to distinguish between facilitated diffusion and active transport.
- Be able to describe why the process requires energy.
- Be able to describe a typical source of energy (general and specific examples).

In some cases it is necessary to move molecules against a gradient. The eukaryotic cell, a typical mammalian cell, has many compartments within the cell each surrounded by a lipid bilayer membrane. In most cases the environment within the compartment is different than that in the cytoplasm. An example is the lysosome, a degradative organelle (membrane bound compartment within the cell) whose function is to digest macromolecules delivered either from the outside of the cell or from other compartments within the cell. To carry out this function the lysosome maintains a much lower pH inside the lysosome relative to the cytoplasm. At equilibrium, the concentration of protons would be equal on both the inside and outside of the lysosome.

### Facilitated Diffusion



Did I Get This?

To decrease the pH inside of the lysosome, the concentration of protons will need to be greater inside the lysosome than in the cytoplasm. To accomplish this protons will need to move from a low concentration to a high concentration. This is a non-spontaneous process and requires the cell to do work to move the ions up-hill against the gradient. To do work, the cell must expend energy and actively move (pump) the ions. This process is referred to as active transport. The source of energy for this process in most biological systems is the hydrolysis of ATP.

### Facilitated Diffusion - continuous process



Did I Get This?



## Facilitated Diffusion

To make the lumen of the lysosome more acidic than the cytoplasm, in which direction would protons need to flow? Why?

Did I Get This?

**Submit and Compare**



## Facilitated Diffusion - continuous process

Why does this need to be a continuous process? Why doesn't the process just stop once the correct pH in the lumen is reached?

Did I Get This?

**Submit and Compare**

The following animation depicts another example of active transport; the sodium-potassium ATPase. This active transport system moves three sodium ions out of the cell and two potassium ions into the cell, each against a gradient.



### Facilitated Diffusion-energy

Did I Get This?

## Transport Proteins

Facilitated diffusion and active transport both require channels or ports in the membrane through which the generally non-permeable molecules can pass. These protein transporters contribute to the mosaic character of the fluid mosaic character of the biological membrane. There are a variety of different structures associated with transport proteins and at the same time many transport proteins that carry out similar functions (e.g. ion channels) have structural similarities while maintaining their ability to discriminate between molecules. Thus transport proteins have been classified both by

## Sodium-Potassium Transporter

## ATP

The energy that cells use is chemical bond energy, the shared electrons that holds atoms together in molecules. Cell movements require energy and chemical reactions are the font of energy in every living cell. Most cell processes use the same energy source: adenosine tri phosphate ATP. The ATP contains three phosphate groups. The bond between the second and third phosphate groups can be broken to release a small amount of energy.

### ATP

An Active antiport transporter

ATP, Adenosine Triphosphate



cartoon model

<http://en.wikipedia.org/wiki/Image:ATP-3D-vdW.png>



## Sodium-Potassium Transporter

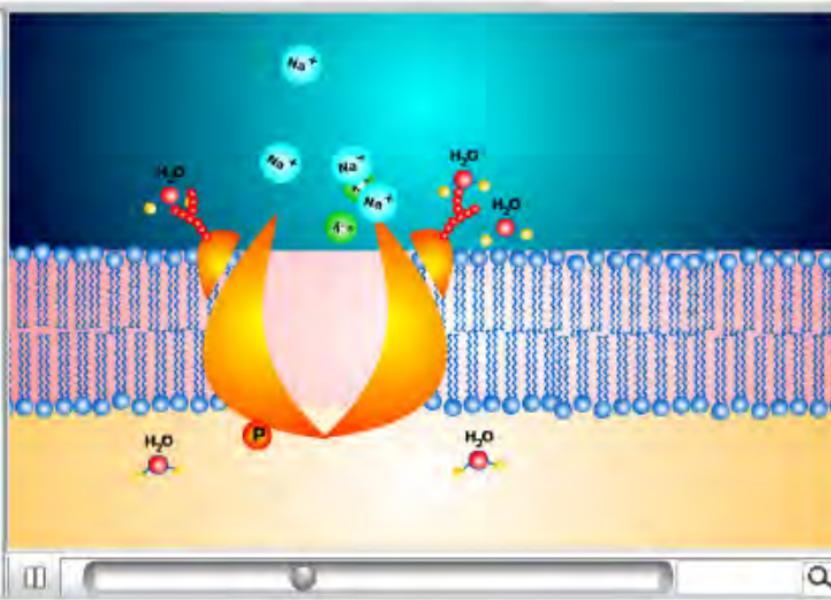
### An Active antiport transporter

This is an example of an antiport transporter than uses the energy of ATP to transport 3 Na<sup>+</sup> ions outside of the cell in exchange for the influx of 2 K<sup>+</sup> ions into the cell. The main features of the cycle are:

- 1) Binding of 3 Na<sup>+</sup> ions
- 2) Phosphorylation of a carboxylic group by ATP, causing an allosteric change in the enzyme, allowing the Na<sup>+</sup> to cross.
- 3) Two K<sup>+</sup> bind to the external face of the transporter.
- 4) Dephosphorylation of the enzyme causes another allosteric change, bringing the K<sup>+</sup> into the cell

ATP

An Active antiport transporter





## Facilitated Diffusion-energy

If ATP hydrolysis provides the energy for the conformational change to move sodium out, what provides the energy for the conformational change required to move the potassium in?

Did I Get This?

Submit and Compare

structure and by function. For the purposes of this course, the classification will be that of function though similarities in structure will be observed in the examples chosen.

There are three classifications of transport proteins based on mechanism of transport: **Uniport**, **Symport** and **Antiport**. The animations on the following pages will demonstrate the three classes of proteins with examples of each.

---

## End of Lesson Questions



My Response

### About Active Transport

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Transport Proteins



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# About Active Transport

Think of two questions about this lesson. These can be for clarification of the material or further insight. Your questions may also shape the discussions in class.

My Question 1 \*

---

My Question 2

---

^ Top ^

# Transport Proteins

[Hide](#)

## Learning Objectives

- **Transport Proteins**

Be able to describe the general structural features of a membrane transport protein.

- **Transport Proteins**

Be able to distinguish the mechanisms of uniports, symports and antiports.

- **Transport Proteins**

Be able to describe a set of criteria for selective transport of a given molecule to pass through a membrane channel.

## Transport Proteins

Facilitated diffusion and active transport both require channels or ports in the membrane through which the generally non-permeable molecules can pass. These protein transporters contribute to the mosaic character of the fluid mosaic character of the biological membrane. There are a variety of different structures associated with transport proteins and at the same time many transport proteins that carry out similar functions (e.g. ion channels) have structural similarities while maintaining their ability to discriminate between molecules. Thus transport proteins have been classified both by structure and by function. For the purposes of this course, the classification will be that of function though similarities in structure will be observed in the examples chosen. There are three classifications of transport proteins based on mechanism of transport: Uniport, Symport and Antiport. The following image illustrates the three classes of proteins with examples of each.

## Carrier Proteins

# Uniport

## Uniport

A uniport is a protein that transports a single molecule across the membrane of the cell.

### Intracellular Transport

The animation below shows how the glucose transporter molecule is structured with a spiral channel that allows the glucose molecules to passively navigate the channel and move through the membrane.

---

*Click the green arrow to play the animation.*

### Intercellular Transport

The simulation below demonstrates how transmembrane protein structures from adjacent cells line up to form Gap Junctions, channels between cells that act as size exclusion transporters. While water molecules are small enough to move through the membranes, the Gap Junctions facilitate that movement and the movement of molecules up to 1500 daltons (approximately a 15 amino acid peptide) but not larger molecules.

## Glucose Transporter

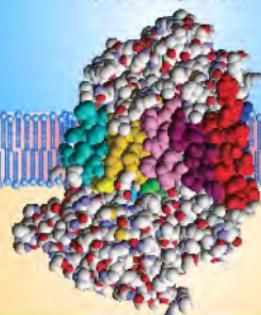
### Glucose transporter

Glucose is an essential substrate for the metabolism of most cells. Because glucose is a polar molecule, its transport through biological membranes requires specific transporter proteins. Down here the structure of the glut1 transporter from different views.

#### Glucose transporter

Begin Simulation

space filling model



Click the green arrow to play the animation.

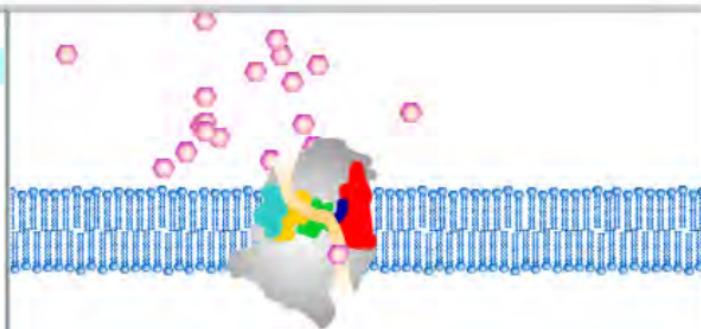
## Glucose Transporter

[Begin Simulation](#)

The Glucose molecules in this example are too large to freely pass through the membrane. This Glucose Transporter allows them through the specific channel through the protein.

Glucose transporter

[Begin Simulation](#)



## Gap Junctions

^ Top ^

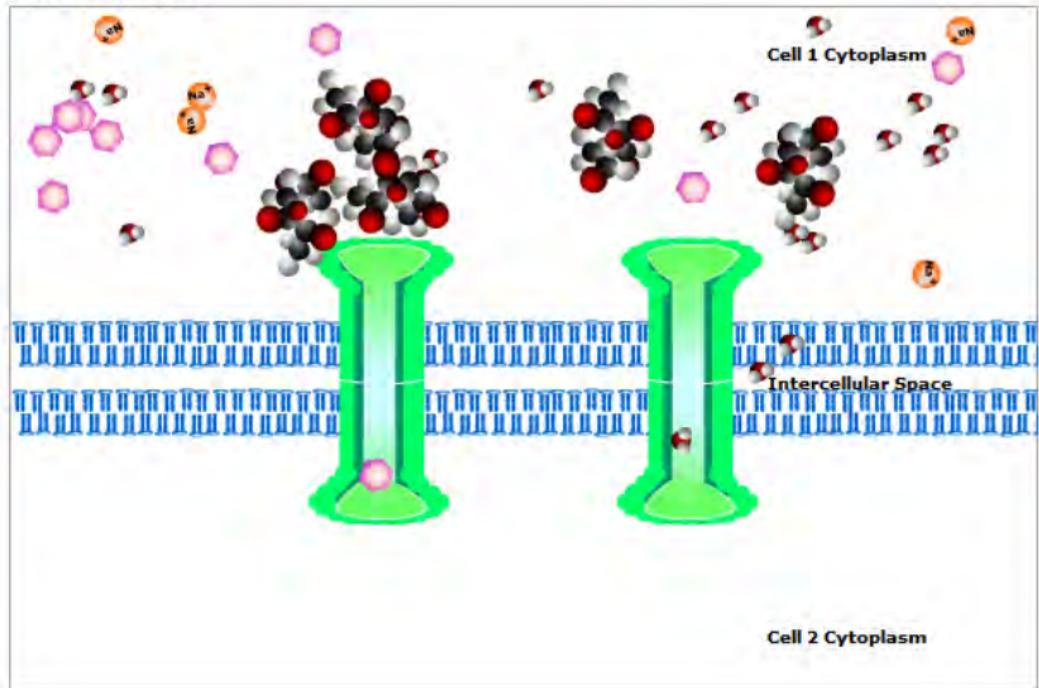
 Symport 

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## Gap Junctions



# Symport

## Symport

A symport transports two different molecules across the membrane in the same direction in a cooperative manner.

---

Click the green arrow to play the animation.

^ Top ^

  Antiport

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## Lactose Permease

## Introduction

The Escherichia coli lactose permease is an example of secondary active transport (Campbell, p. 210). This enzyme is similar in structure to others in the major facilitator superfamily (MFS) of transporters. More than 1000 examples of MFS transporters have been identified in the genomes of bacteria, plants, and animals.

### Introduction

#### Lactose Permease Mechanism:

Lac Permease structure

Proton Binds

Lactose Binds

Structural Change

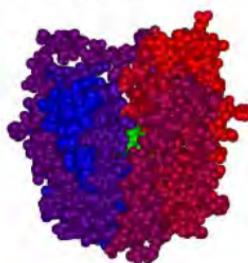
Lactose Dissociates

Proton Dissociates

Return to Start

space-filling model - side view

click play  
to see the  
top view



Click the green arrow to play the animation.

## Lactose Permease

## Lactose Permease Mechanism:

Lactose permease (*lacY* gene product) is a  $\beta$ -galactoside-H $^{+}$  symporter. The high H $^{+}$  concentration in the *E. coli* periplasm is used to drive the transport of lactose into the cell against its concentration gradient. The proton gradient is generated by the oxidation of substrates via the proton pumping of the electron transport chain.

[Introduction](#)

### Lactose Permease Mechanism:

[Lac Permease structure](#)

[Proton Binds](#)

[Lactose Binds](#)

[Structural Change](#)

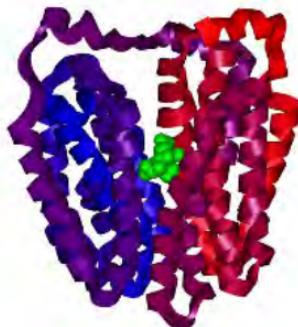
[Lactose Dissociates](#)

[Proton Dissociates](#)

[Return to Start](#)

ribbon model

click play  
to see  
other  
models



Click the green arrow to play the animation.

## Lactose Permease

## Lac Permease structure

The enzyme, in its substrate-free form is shown in cross-section with the periplasm at the top of the diagram. The cavity between the N- and C-terminal domains contain the substrate and H<sup>+</sup> binding sites.

[Introduction](#)

[Lactose Permease Mechanism:](#)

[Lac Permease structure](#)

[Proton Binds](#)

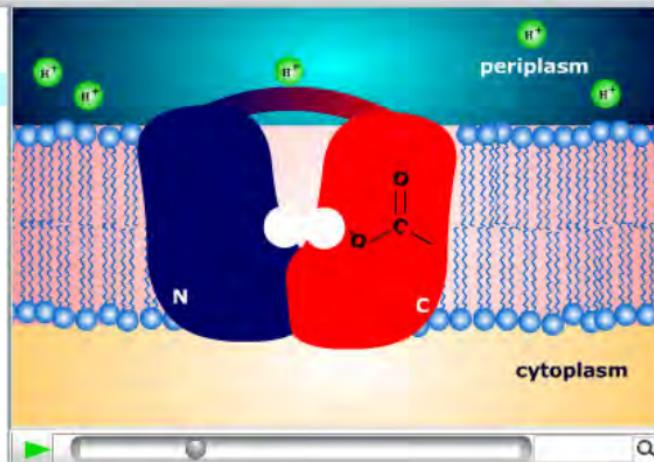
[Lactose Binds](#)

[Structural Change](#)

[Lactose Dissociates](#)

[Proton Dissociates](#)

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## Lactose Permease

## Proton Binds

Proton binding to a glutamic acid sidechain in the C-terminal domain (-COO-) is the first step. The carboxyl group of this Glu residue is in a hydrophobic environment making this protonation energetically favorable ( $pK_a \sim 7.0$ ).

[Introduction](#)

[Lactose Permease Mechanism:](#)

[Lac Permease structure](#)

[Proton Binds](#)

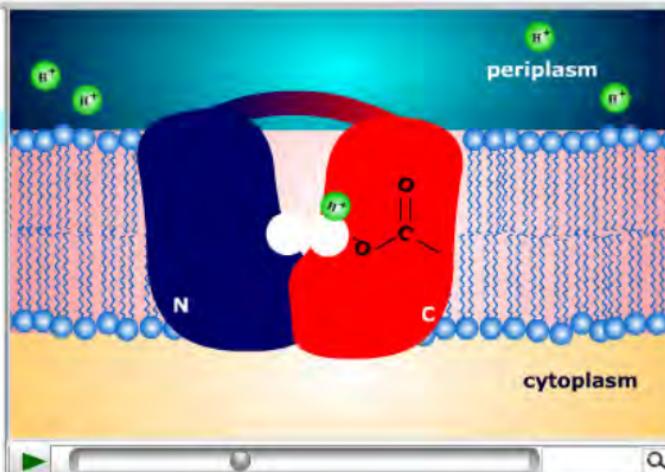
[Lactose Binds](#)

[Structural Change](#)

[Lactose Dissociates](#)

[Proton Dissociates](#)

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## Lactose Permease

## Lactose Binds

Substrate binding is the second step. The sugar binds primarily to residues in the N-terminal domain at the bottom of the cavity, roughly halfway between the bilayer boundaries.

[Introduction](#)

**Lactose Permease Mechanism:**

[Lac Permease structure](#)

[Proton Binds](#)

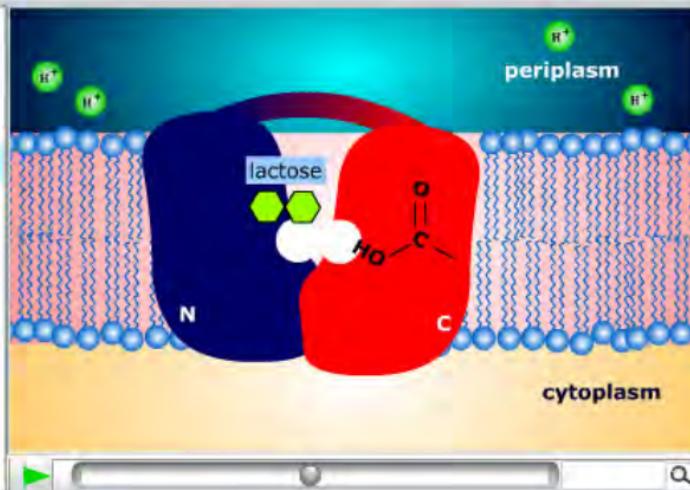
[Lactose Binds](#)

[Structural Change](#)

[Lactose Dissociates](#)

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## Lactose Permease

## Structural Change

Substrate binding also triggers a major conformation change: The periplasmic opening closes and the cavity appears on the cytoplasmic side, i.e. the opening switches to the other side, but the protein, itself, does not "flip" across the membrane

[Introduction](#)

[Lactose Permease Mechanism:](#)

[Lac Permease structure](#)

[Proton Binds](#)

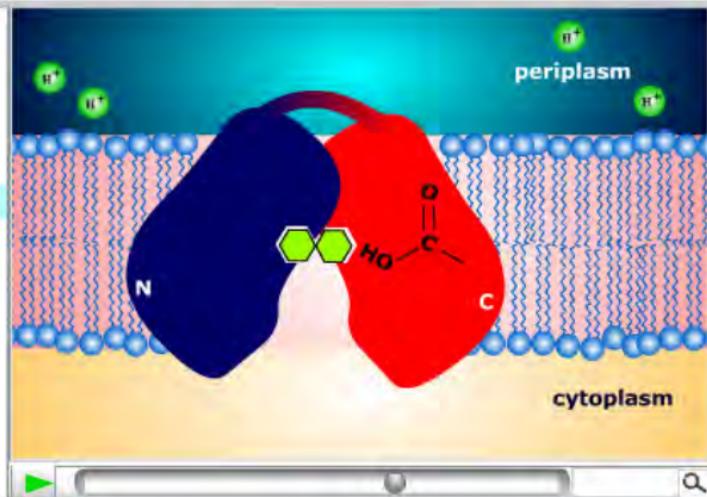
[Lactose Binds](#)

[Structural Change](#)

[Lactose Dissociates](#)

[Proton Dissociates](#)

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## Lactose Permease

## Lactose Dissociates

The disaccharide substrate dissociates into the cytoplasm where it will be hydrolyzed (by  $\beta$ -galactosidase) and used for energy production or other metabolic purposes.

[Introduction](#)

[Lactose Permease Mechanism:](#)

[Lac Permease structure](#)

[Proton Binds](#)

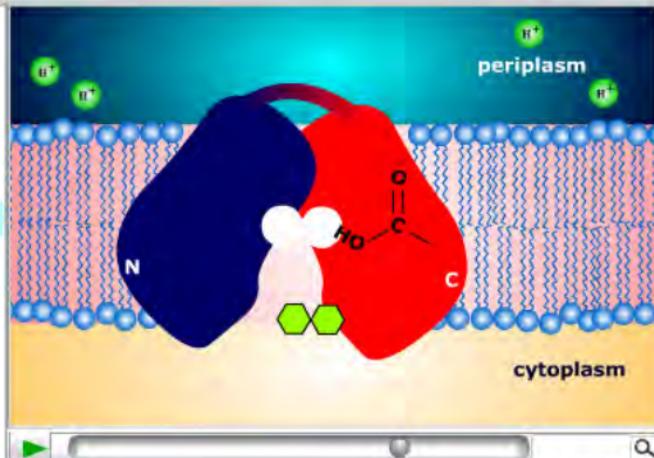
[Lactose Binds](#)

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[Lactose Dissociates](#)

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## Lactose Permease

## Proton Dissociates

The H<sup>+</sup> dissociates after the substrate. This too is a spontaneous reaction because the conformation change has also made the environment of the Glu side chain more polar, lowering its pKa.

### Introduction

#### Lactose Permease Mechanism:

Lac Permease structure

Proton Binds

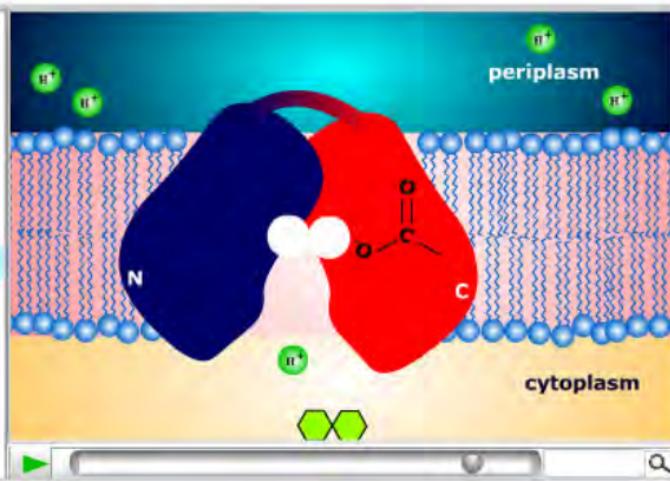
Lactose Binds

Structural Change

Lactose Dissociates

Proton Dissociates

Return to Start



## Lactose Permease

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In the absence of substrate and H<sup>+</sup> in the active site, the permease is more stable in its original state. Hence, the reverse of the major conformation change returns the protein to its starting conformation for another cycle of lactose-H<sup>+</sup> symport.

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[Lactose Permease Mechanism:](#)

[Lac Permease structure](#)

[Proton Binds](#)

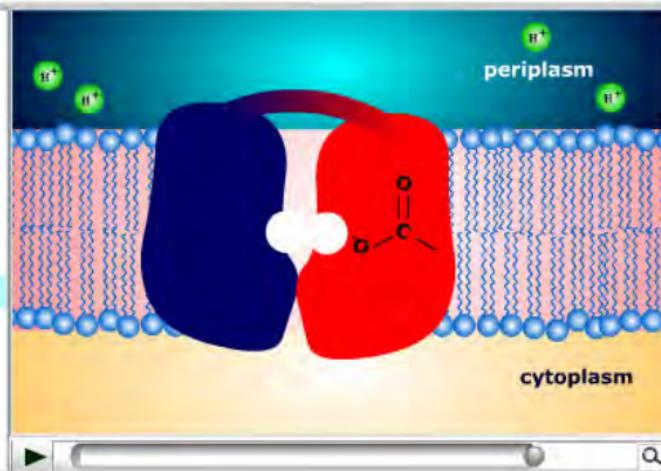
[Lactose Binds](#)

[Structural Change](#)

[Lactose Dissociates](#)

[Proton Dissociates](#)

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# Antiport

## Antiport

Antiports transport two different molecules through the membrane in opposite directions.



## Facilitated Diffusion Active Transport

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 Introduction 

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## ADP-ATP exchange

### Structure

The mitochondrial ADP/ATP translocase (AAT) catalyses the exchange, across the inner membrane of the organelle, of cytosolic ADP for ATP, produced in the matrix by ATP-synthase. The AAT undergoes substantial conformational changes during transport. Down here different models of the AAT structure from different views.

#### Structure

ADP-ATP exchange

mitochondria

phase 1

phase 2



ribbon model



## ADP-ATP exchange

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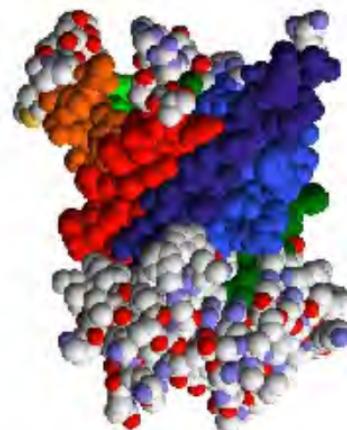
### Structure

ADP-ATP exchange

mitochondria

phase 1

phase 2



space filling  
model



## ADP-ATP exchange

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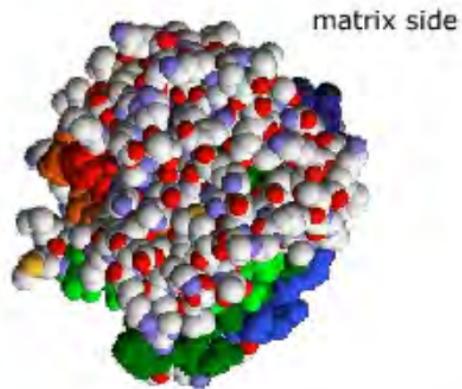
#### Structure

ADP-ATP exchange

mitochondria

phase 1

phase 2



## ADP-ATP exchange

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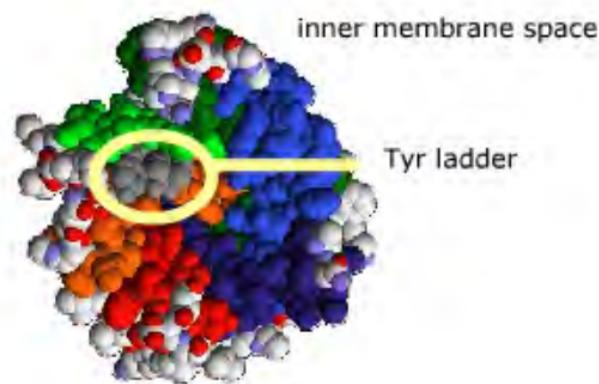
### Structure

ADP-ATP exchange

mitochondria

phase 1

phase 2



## ADP-ATP exchange

## ADP-ATP exchange

Proteins of the mitochondrial carrier family are embedded in this membrane, and each member of the family achieves the selective transport of a specific metabolite. Among these, the ADP/ATP carrier transports ADP into the mitochondrial matrix and exports ATP toward the cytosol after its synthesis.

### Structure

#### ADP-ATP exchange

mitochondria

phase 1

phase 2

The cell



## ADP-ATP exchange

## ADP-ATP exchange

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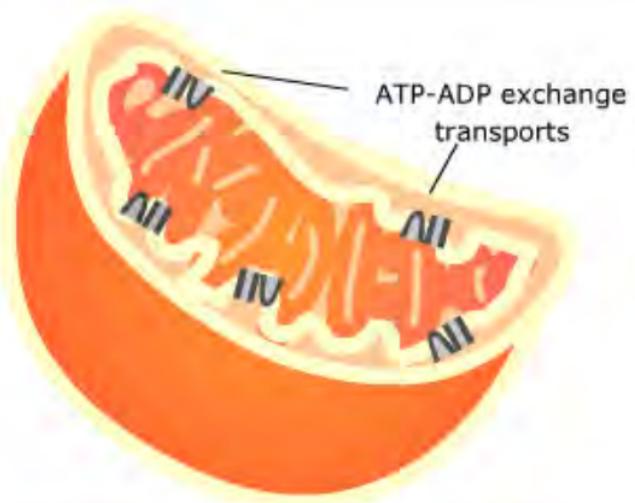
### Structure

#### ADP-ATP exchange

mitochondria

phase 1

phase 2



## ADP-ATP exchange

### phase 1

The dimer structure of the ADP/ATP carrier presents the structure of the molecule that accepts ADP into the closed cup conformation of the protein while the dimer pair in the open conformation binds ATP. Following binding each member of the dimer pair undergoes a conformational change that the releases the bound molecule on the opposite side of the membrane.

#### Structure

ADP-ATP exchange

mitochondria

phase 1

phase 2

#### inner membrane space



#### matrix



## ADP-ATP exchange

### phase 1

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Structure

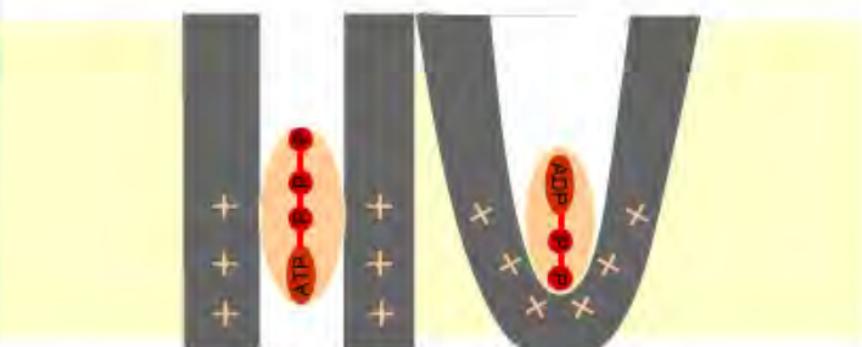
ADP-ATP exchange

mitochondria

phase 1

phase 2

inner membrane space



matrix



## ADP-ATP exchange

### phase 1

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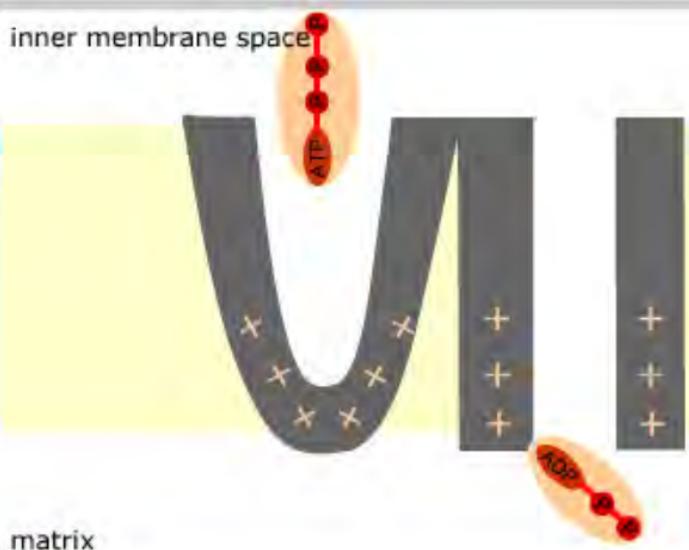
Structure

ADP-ATP exchange

mitochondria

phase 1

phase 2



matrix



## ADP-ATP exchange

### phase 2

Having completed the first exchange reaction, the opposite member of the dimer pair is ready to undertake the transfer reaction. Again the cup structure binds the ADP while the open structure binds ATP. Conformational change then releases the ADP to the matrix and ATP to the inner membrane space.

Structure

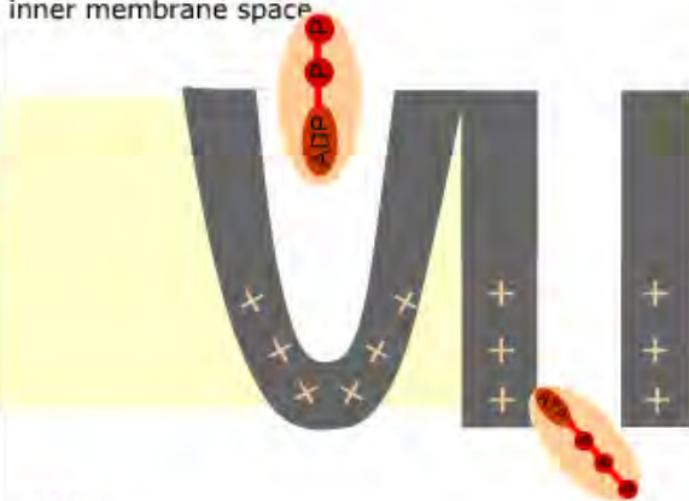
ADP-ATP exchange

mitochondria

phase 1

phase 2

inner membrane space



matrix



## ADP-ATP exchange

### phase 2

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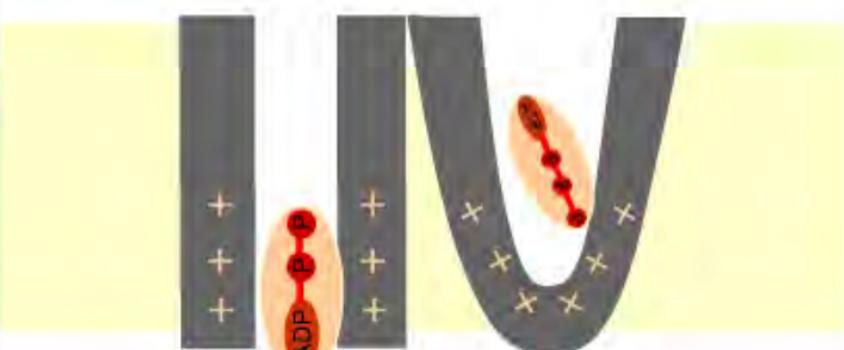
ADP-ATP exchange

mitochondria

phase 1

phase 2

inner membrane space



matrix



# Facilitated Diffusion Active Transport

## Question 1

Active transport is facilitated diffusion\_\_\_\_\_.

Select one answer.

- A. against a concentration gradient
- B. that is indiscriminant as to the transported ligand
- C. that moves molecules down the concentration gradient.

Check your answers

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Jump to 1 of 7

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# Facilitated Diffusion Active Transport

## Question 2

The gap junction is an example of a uniport that discriminates based on

Select one answer.

- A. shape
- B. size
- C. charge
- D. polarity
- E. all of the above

Check your answers

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# Facilitated Diffusion Active Transport

## Question 3

Facilitated diffusion can be discriminating based on

Select one answer.

- A. shape
- B. size
- C. charge
- D. polarity
- E. all of the above

Check your answers

^ Top ^

Jump to 3 of 7

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Next

# Facilitated Diffusion Active Transport

## Question 4

Coordinated transport of two molecules in the opposite directions through a channel uses  
a(n) Select one answer.

- A.** uniport
- B.** symport
- C.** antiport

[Check your answers](#)

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Jump to 4 of 7

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# Facilitated Diffusion Active Transport

## Question 5

Coordinated transport of two molecules in the same direction through a channel uses  
a(n)

Select one answer.

- A.** uniport
- B.** symport
- C.** antiport

Check your answers

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# Facilitated Diffusion Active Transport

## Question 6

Transport of a single molecule through a channel uses a(n)

Select one answer.

- A. uniport
- B. symport
- C. antiport

Check your answers

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Jump to 6 of 7

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# Facilitated Diffusion Active Transport

## Question 7

Facilitated diffusion is generally described as indiscriminant transport of molecules across a lipid bilayer

Select one answer.

- A. True
- B. False

Check your answers

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Jump to 7 of 7

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 Next 



# Introduction

[Hide](#)

## Learning Objectives

- Be able to describe the difference between general endocytosis and protein transduction.
- Be able to describe the difference between pinocytosis and phagocytosis.
- Be able to describe the fate of the material undergoing endocytosis.
- Be able to describe how the inside surface of the endocytic vesicle is the same as the outside surface of the cell and why that is important to the cell.

## Endocytosis

While facilitated diffusion and active transport account for a great deal of the specific uptake of molecules and ions needed by the cell, other sources of external matter can also be taken up by the cell. The channels and pores provide a means by which molecules can pass directly through the membrane to the cytoplasm. Other mechanisms also exist by which molecules are taken up by the cell but do not directly pass through the plasma membrane. This mechanism is referred to as **endocytosis**. This mechanism involves the engulfing of the matter by the plasma membrane and internalization of the engulfed material inside a cytoplasmic vesicle. Non-specific uptake of molecules occurs by **phagocytosis** (large particles and macromolecules) and **pinocytosis** (water soluble small molecules).

In general endocytosis, a molecule or particle encounters the cell surface and randomly causes the membrane to create first a pit in the membrane, followed by a further invagination of the plasma membrane and finally the pinching off of the plasma membrane around the molecule or particle resulting in the formation of a vesicle in the cytoplasm of the cell. Note that during the process the asymmetry of the membrane would be apparent by the fact that the inside surface of the newly formed vesicle is the same as the exterior surface of the cell. Thus the integrity of the cytoplasm and its exposure to only the inside surface of the membrane is preserved. **Exocytosis** is just the reverse of this process with the fusion of an internal vesicle with the plasma membrane thus releasing its content to the outside. The balance of exocytosis and endocytosis preserves the size of the plasma membrane and ensure neither growth nor shrinking of the cell size.

Once internalized the new vesicle fuses with a slightly acidic early endosome and subsequently with the lysosome where the contents of the original endocytic vesicle are digested and the digested products released to the cytoplasm where they are available for use by the cell. This process is depicted in the following animation.

---

*You can use the magnifier in the lower right-hand corner to zoom the animation*

### **Protein Transduction – an example of macropinocytosis**

In the early 1990's an intriguing observation was made that has lead to a number of new approaches to drug delivery and therapeutic delivery systems. It is based on an observation of the activity of the transactivator TAT protein associated with the human immunodeficiency virus (HIV-1) and subsequently polyarginine (arginine is a positively charge, naturally occurring amino acid) and other proteins containing a basic peptide region referred to as the protein transduction domain (PTD). The observation was the translocation of virtually any molecule, particle, even liposome that has the PTD attached. While there is still some debate as to the exact mechanism of the translocation, there is some agreement on the general process. The highly positively charged PTD, attached to its 'cargo', has a tight electrostatic (ionic) interaction with certain molecules, which are ubiquitous to all cells, in the plasma membrane. Binding to the surface initiates macropinocytosis (pinocytosis with a slightly larger soluble molecule). The presence of the PTD provides for high efficiency initiation of endocytosis. While not involving a specific receptor, the binding by the PTD to the cell surface reduces the concentration dependence for initiation of internalization.

You can use the magnifier in the lower right-hand corner to zoom the animation



Did I Get This?

## Endocytosis

In contrast to the normal endocytic vesicle the PTD directed endocytic vesicle undergoes retrograde transport. In this process the new vesicle fuses with the Golgi and is the PTD containing proteins are transported back to the Rough Endoplasmic Reticulum where they undergo post-translational modification and are transduced directly to the cytoplasm.

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[←](#) Receptor Mediated Endocytosis [→](#)

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## Endocytosis

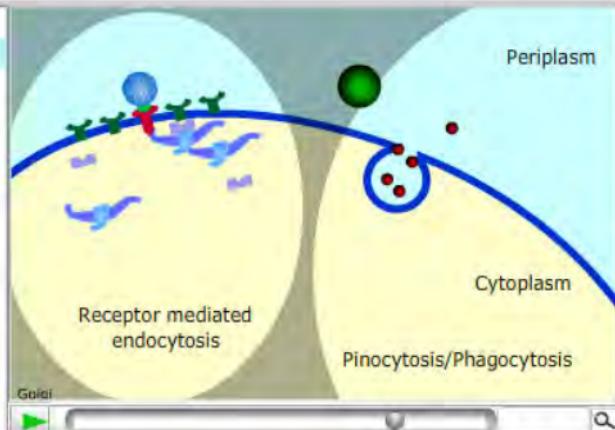
## Describe/Endocytosis

Pinocytosis and phagocytosis are both types of endocytosis. Pinocytosis is cellular drinking and phagocytosis is cellular eating.

Receptor mediated endocytosis is a process by which cells internalize molecules or viruses. As its name implies, it depends on the interaction of that molecule with a specific binding protein in the cell membrane called a receptor.

Introduction

Describe/Endocytosis



## Endocytosis

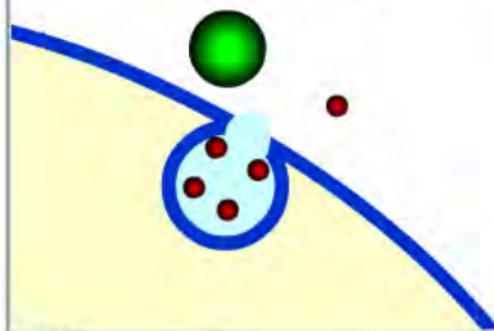
## Introduction

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### Introduction

#### Describe/Endocytosis

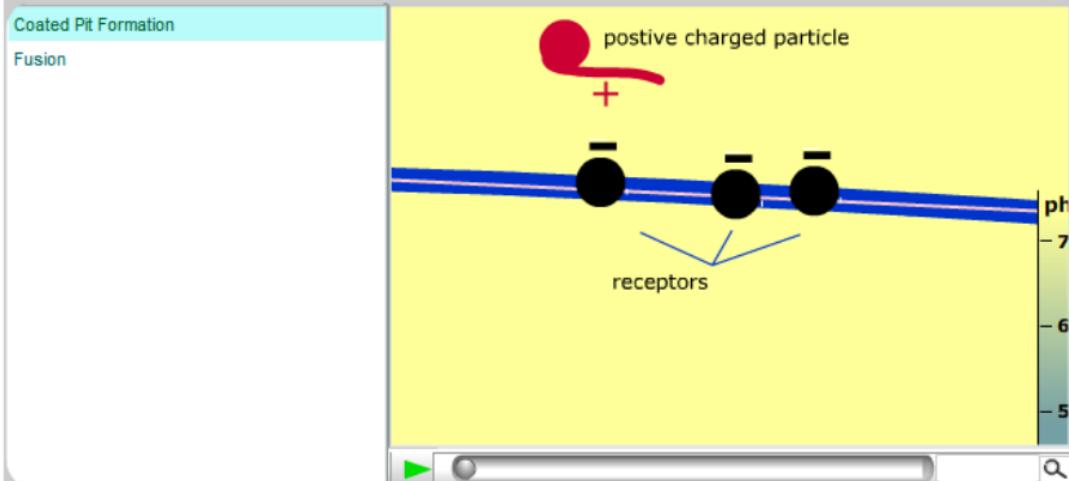
## Pinocytosis Phagocytosis



## Macro-Pinocytosis

## Coated Pit Formation

This simulation describes the process of Receptor Mediated Endocytosis that involves all of the components illustrated on the stage in the lower right panel. Each component is labeled and will be introduced as the simulation proceeds. The lower left panel provides a breakdown of the steps involved and the green play arrow advances the animation through the separate steps providing a simulation of each step. It is possible to repeat a step by clicking on the name of that step in the lower left panel.



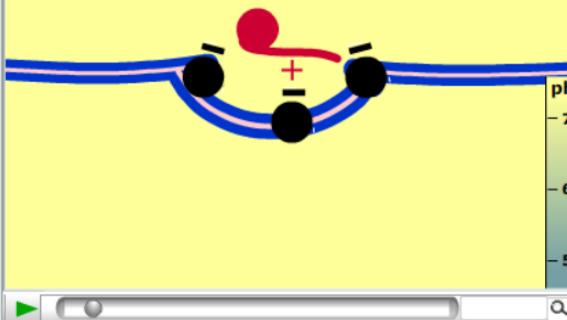
## Macro-Pinocytosis

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### Coated Pit Formation

Fusion



You can use the magnifier in the lower right-hand corner to zoom the animation



## Endocytosis

What would the characteristics of the surface molecule need to be for tight binding to the PTD?

Did I Get This?

**Submit and Compare**

# Receptor Mediated Endocytosis

[Hide](#)

## Learning Objectives

- Be able to describe how receptor mediated endocytosis differs from phagocytosis.
- Be able to describe how receptor mediated endocytosis differs from protein transduction.
- Be able to describe the fate of a molecule taken into a cell by receptor mediated endocytosis.
- Be able to describe environmental changes necessary to allow recycling of intermediates in receptor mediated endocytosis.

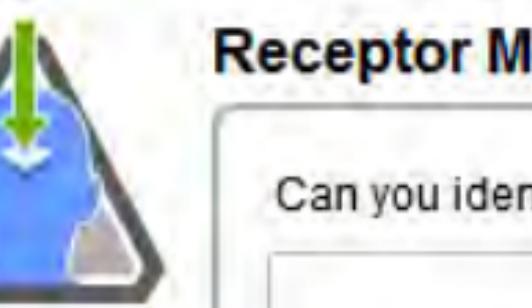
## Receptor Mediated Endocytosis

Much as the channels and pores discriminate between specific molecules and their transport through the membrane, specificity and discrimination are seen during endocytosis using specific membrane bound receptors. This targeting defines the uptake of specific molecules or assemblies by specific cells. The following animation demonstrates the process of receptor mediated endocytosis for the Low Density Lipoprotein (LDL) complex. The process is divided into the individual steps to emphasize similarities and differences among general endocytosis, protein transduction and receptor mediated endocytosis. Several general concepts are illustrated during the process including bioselectivity and intermediate recycling.

### Receptor Mediated Endocytosis



Did I Get This?



## Receptor Mediated Endocytosis

Can you identify where each of these concepts contributes to the process?

Did I Get This?

**Submit and Compare**

## Receptor Mediated Endocytosis

### Overview

Many macromolecules are taken into the cell by a process described as endocytosis. The macromolecules do not pass through the membrane directly to the cytoplasm but instead are taken up by the cell, processed by cell and then delivered to the cytoplasm. For many of the endocytic processes, the uptake of the molecule is very specific and is controlled by recognition of the molecule by a specific receptor on the surface of the cell. This process is called Receptor Mediated Endocytosis.

This simulation describes the process of Receptor Mediated Endocytosis that involves all of the components illustrated on

#### Overview

[Zoom in](#)

[LDL particle](#)

[Equilibrium](#)

[Coated Pit Formation](#)

[Endocytosis](#)

[Uncoated Vesicle Formation](#)

[Fusion with endosome](#)

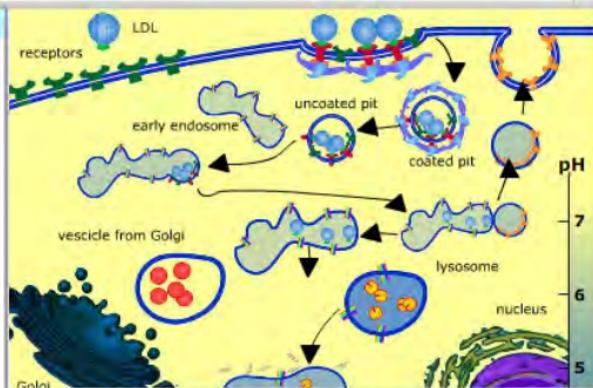
[Receptors recycling](#)

[Formation of a new vesicle](#)

[Fusion](#)

1) with a Golgi vesicle

2) with a lysosomeX





# Signal Transduction

The plasma membrane is a very selective barrier. We have seen how some small molecule pass freely, but most molecules are selectively brought into the cells using transporter proteins. Most of these small molecules are metabolites or ions used in the general metabolism of the cell. The cell also needs to transduce information across its membrane. Cells receive signals from the surrounding fluids and other cells. These signals may tell the cell to divide or prevent division and promote growth.

The animation below demonstrates the action of signal transduction through a G-Protein coupled receptor. The ligand is the external signal and it binds the receptor. The G-Protein complex is now able to bind to the receptor. This activates the G-protein by allowing the exchange of GTP for GDP. When bound to GTP the G-protein is able to bind to Adenylate cyclase and activate it. Adenylate cyclase generates the internal signal that is then interpreted by the cell.



## Endocytosis/Signal Transduction

Did I Get This?

## End of Lesson Questions



My Response

### About Signaling

## Graded Quiz

The following quiz will be graded and recorded in the grade book. You may take this quiz only once.



Quiz

### Membrane Transport

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[Organelles \(new for CC-OLI\)](#)

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# Endocytosis/SignalTransduction

## Question 1

The LDL receptor is the only known example of receptor mediated endocytosis.

Select one answer.

- A. True
- B. False

## Question 2

Signal transduction involves all of the following except

Select one answer.

- A. G-protein
- B. GTP/GDP exchange
- C. enzyme activation
- D. pH control of conformational change
- E. ligand recognition by a specific receptor

## Question 3

Signal transduction involves several distinct equilibrium controlled reactions.

Select one answer.

- A. True
- B. False

## Question 4

Receptor mediated endocytosis exhibits all of the following except

Select one answer.

- A. discrimination in recognition
- B. recycling and reuse of materials
- C. pH control of degradation
- D. use of a static set of structures
- E. conformation change associated with binding.

## Question 5

Protein transduction involves all of the following except

Select one answer.

- A. transfer of large macromolecules (cargo) into a cell in a vesicle.
- B. Recognition of the molecule to be taken into the cell by a positively charged signal sequence.
- C. delivery of the material to internal organelles.
- D. passage of the particle/macromolecule directly through the membrane lipid bilayer.
- E. recycling of the vesicle to the surface.

## Question 6

Pinocytosis involves the capture and engulfing of macromolecules and particles.

Select one answer.

- A. True
- B. False

## Question 7

Endocytosis involves all of the following except

Select one answer.

- A. formation of a clathrin coated pit.
- B. fusion of the membrane around the external material.
- C. transfer of the molecule directly through the membrane lipid bilayer.
- D. fusion of the envaginated vesicle with internal organelles.

Check your answers

^ Top ^

Close

# About Signaling

Think of two questions about this lesson. These can be for clarification of the material or further insight. Your questions may also shape the discussions in class.

My Question 1 \*

---

My Question 2

---

^ Top ^

# Membrane Transport

## Question 1

Clathrin is a cytoskeleton type assembly formed around the vesicle during endocytosis.

- A. true
- B. false

Select one answer.

*10 points*

## Question 2

Receptor mediated endocytosis

- A. delivers specific molecules to compartments of the cell initiated by binding to a complementary receptor.
- B. specifically endocytosis an exogenous molecule to be recycled to the surface
- C. involves extensive protein synthesis to regenerate the receptor after its degradation by the process.
- D. involves the lysosome strictly as a transport vesicle.

Select one answer.

*10 points*

## Question 3

Spilled perfume moves from one side of the room to the other by

- A. osmosis
- B. diffusion
- C. bulk flow
- D. turgor pressure
- E. active transport

Select one answer.

*10 points*

## Question 4

Lipid soluble, small molecules such as urea, DMSO, and alcohol pass across the cell membrane via

- A. facilitated diffusion
- B. active transport

Select one answer.

*10 points*

- C. osmosis
- D. phagocytosis
- E. simple diffusion

## Question 5

Glucose and amino acids are passively transported through the bacterial cell membrane via

Select one answer.  
*10 points*

- A. facilitated diffusion
- B. active transport
- C. osmosis
- D. phagocytosis
- E. receptor mediated endocytosis

## Question 6

Of the following molecules, which is most likely to enter a cell by simple diffusion through the lipid bilayer?

Select one answer.  
*10 points*

- A. calcium ion
- B. an amino acid at neutral pH
- C. water
- D. glucose

## Question 7

Penicillin is toxic to new bacterial cells because it prevents cell wall formation, causing the cells to burst. This indicates that the bacteria live in

Select one answer.  
*10 points*

- A. hypotonic medium
- B. hypertonic medium
- C. isotonic medium

## Question 8

If a cell is placed in an isotonic solution, which of the following will occur?

Select one answer.

10 points

- A. There will be a net movement of salts into the cell from the surrounding solution.
- B. There will be a net movement of water into the cell from the surrounding solution
- C. There will be a net movement of salts out of the cell into the surrounding solution
- D. There will be a net movement of water out of the cell into the surrounding solution.
- E. none of the above

## Question 9

In signal transduction, the intermediary between the transducer and the final molecule to be activated is

Select one answer.

10 points

- A. ATP
- B. G-protein
- C. adenyl cyclase
- D. the ligand

## Question 10

Movement of molecules through the transport proteins is driven by \_\_\_\_\_ unless \_\_\_\_\_ is supplied.

Select one answer.

10 points

- A. osmotic pressure; water
- B. simple diffusion; energy
- C. endocytic pressure; ligand

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# Organelles (new for CC-OLI)

[Hide](#)

## Learning Objectives

- List the major organelles of the cell and state the associated function(s). Roughly enumerate the organelles per cell. Synthesize ideas regarding differential organelle number in specialized cells.

The diversity of life began when membranes enclosed packets of self-replicating molecules, thus providing a protected medium buffered against environmental changes outside. Besides enclosing the cell, membranes act as guardians of the cell, permitting passage of molecules in and out. Membranes also serve within the cell as the structural components of organelles. Membranes are typically comprised of two layers of lipid fat. Most proteins interact with membranes in some way. Within the layers, often stretching across, are embedded proteins and other macromolecules. These proteins govern much of the cell's interaction with its environment. Malfunctions in membrane proteins can have severe consequences. For example, cystic fibrosis is caused by a gene mutation that impairs functioning of a chloride ion channel protein. Membranes harbor other molecules, such as carbohydrates, which play role in immune responses.

[^ Top ^](#) Metabolism (new for CC-OLI) 

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# Metabolism (new for CC-OLI)

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## Learning Objectives

- Describe physiological events that would lead to cellular proliferation. List the steps of mitosis and cytokinesis and identify key cellular features related to the steps of proliferation.

Without metabolism, life would not be able to divert energy to overcome entropy – the tendency to disorder. Broadly speaking it is the entire set of chemical reactions that allow organisms to maintain homeostasis. One of the key roles of metabolism is to harvest energy from food. The body uses this energy to drive chemical reactions necessary for various cellular processes. Digestive processes convert food into the simple sugar glucose, which is then broken down via a complex chemical process – the citric acid cycle. At various points in the cycle, oxygen is used from respiration to incorporate the energy from glucose into a nucleotide molecule, adenosine triphosphate or ATP. The ATP produced via this process of glycolysis is the molecular currency that runs the cellular economy. Catabolism, the breakdown of complex molecules, provides the energy for anabolism, synthesizing of complex molecules from simple precursors, and hence the continuation and cycles of life.

[^ Top ^](#)  [Metabolism](#)

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# Metabolism

Living organisms consume food, in the form of carbohydrates, fats, and amino acids, to live. The process of metabolism breaks these complex biomolecules into simple molecules with the release of energy. The most common form of energy is adenosine triphosphate (ATP). This high energy phosphorylated compound is used as an energy source in many cellular processes and for biomechanical functions, such as muscle contraction or ion transport across membranes. The resultant compounds and energy released from food are used to synthesize complex molecules for the specialized needs of the cell or organism.

The transformation of ingested food to energy and simple compounds, or the synthesis of complex molecules, is performed by a series of enzymatic reactions. Collectively, these enzymes, and their substrates and products, are referred to as a **metabolic pathway**.

Degradative or **catabolic** pathways generally release energy and electrons from oxidative processes, i.e.



the electrons, which are carried on organic electron carriers, can be used to generate additional energy, or can be used for synthetic purposes.

Synthetic, or **anabolic** pathways consume energy and are generally reductive, requiring electrons.

In this section of the course we will investigate in some detail the production of energy from glucose and how this process is regulated to maintain homeostasis. Since the entire process of metabolism is complex, it is useful to discuss the general features of the metabolic pathways that are involved in converting sugars, amino acids, and fats to energy. Important features of pathways include:

1. input and output compounds,
2. the cellular location of the pathway,
3. the type of energy the pathway produces.

- **Sugars** are degraded as follows:
  - **Glycolysis** is the first pathway used to degrade sugars and it is located in the **cytoplasm**. The simple monosaccharide, glucose, is considered to be the entry point to this pathway. The three carbon keto acid, **pyruvate**, is the final product of glycolysis. Glycolysis generates a small amount of energy in the form of the high energy compound ATP and high energy electrons, carried on organic electron carriers. These electrons are brought into the mitochondria.
  - The **citric acid cycle**, or tricarboxylic acid cycle (TCA), is the second pathway in the degradation of sugars. It is located in the matrix of the mitochondria. Pyruvate enters the TCA cycle by loss of CO<sub>2</sub> to produce a key metabolic intermediate, **acetyl-CoA**. The remaining two carbons from pyruvate are lost as carbon dioxide in the TCA cycle. The energy released by these oxidations is stored on high-energy electron carriers.
  - The **electron transport chain** consists of a number of proteins that exist as four distinct complexes in the inner membrane of the mitochondria. This pathway takes the electrons

from the high energy electron carriers and deposits them on oxygen, generating water. This releases energy, which is used to produce a high concentration of protons, or a **proton gradient** across the inner mitochondrial membrane.

- **ATP synthase**, which is final step in energy generation, utilizes the proton gradient to synthesize ATP. This multi-protein enzyme complex also resides in the inner mitochondrial matrix.
- **Amino Acids** are largely degraded by entry into the TCA cycle, followed by electron transport, and finally ATP synthesis from the proton gradient.
- **Fats**, in the form of triglycerides, are first broken down into glycerol and fatty acids. The fatty acids are oxidized by the beta-oxidation pathway, which converts the carbon in the fatty acid to Acetyl-CoA. The acetyl-CoA enters the TCA cycle, this is again followed by electron transport, and then ATP synthesis.

The location and connections between these degradative pathways is shown below:

## Metabolism Overview

---

**CLICK ON THE RADIO BUTTONS** to show the flow of carbon atoms, electrons, and protons through each pathway. **Overview of Metabolism:** The four key pathways, glycolysis, the TCA cycle, electron transport, and ATP synthesis are outlined in yellow. Glucose that is brought into the cell via the glucose transporter can suffer two fates, oxidation or storage as glycogen. Oxidation occurs in glycolysis and the TCA cycle, releasing the carbon atoms in glucose as CO<sub>2</sub>. Note that oxygen is not used until the end of the electron transport chain. High energy electrons, symbolized as orange balls are carried on organic electron carriers to the electron transport chain. As these electrons move through the four complexes, protons are pumped from the mitochondrial matrix across the inner mitochondrial membrane. As these protons flow back through the membrane via ATP synthase, ATP is generated.

Many of these pathways, with minor modifications, are reversed for synthetic purposes. For example, glucose can be synthesized from pyruvate, fatty acids from acetyl-CoA, and amino acids

from intermediates in the TCA cycle.



Did I Get This?

## Introduction to Metabolism

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Metabolic Pathways

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# Introduction to Metabolism

## Question 1

The correct order of pathways for the oxidation of glucose is:

Select one answer.

- A. TCA cycle, e-transport, ATP synthesis, glycolysis
- B. glycolysis, beta-oxidation, e-transport
- C. glycolysis, TCA cycle, e-transport
- D. glycolysis, TCA cycle, e-transport,ATP synthesis
- E. beta oxidation, TCA cycle, e-transport

## Question 2

The carbon atoms in glucose are released as CO<sub>2</sub> in which pathway?

Select one answer.

- A. Glycolysis
- B. TCA cycle
- C. Electron transport

## Question 3

Which of the following pathway(s) occur in the inner mitochondrial membrane?

Select all that apply.

- A. Glycolysis
- B. TCA cycle
- C. electron transport
- D. ATP synthesis

## Question 4

The energy contained in high energy electrons is used to:

Select one answer.

- A. generate ATP.
- B. transport protons into the mitochondrial matrix.
- C. transport protons out of the mitochondrial matrix

- D. transport protons out of the cell

## Question 5

A first intermediate that is found in both glucose and fatty acid oxidation is

Select one answer.

- A. citrate
- B. pyruvate
- C. acetyl-CoA

Check your answers

^ Top ^

Close

# Metabolic Pathways

[Hide](#)

## Learning Objectives

By the end of this module, students should be able to:

- State the major differences between catabolic and anabolic pathways.
- Describe the common features of metabolic pathways.
- Describe a linear, branched, and circular pathway.

Degradative, or **catabolic**, pathways generally produce energy. They usually begin with a number of different compounds, each of which represents a branch at the beginning of the pathway. These branches meet at a common intermediate, and the remaining section of the pathway is usually a linear segment. In this way a number of complex compounds are converted to a common intermediate, reducing the number of unique steps in the degradation of complex molecules.

Synthetic, or **anabolic**, pathways generally consume energy. They usually consist of an initial linear segment, followed by branching to complex compounds at the end of the pathway. This strategy allows the use of common simple starting materials for the synthesis of a number of complex molecules.

Common features of all metabolic pathways are:

1. They contain multiple intermediates (e.g. compounds A, B, C, ....), with small molecular differences between the intermediates.
2. Each step, or conversion between intermediates, is catalyzed by an enzyme (e.g. E<sub>1</sub>).
3. The pathway is regulated to optimize the use of resources.

It is possible to reverse the direction of a metabolic pathways, depending on the needs of the organisms; a degradative pathway can become a synthetic one. Many of the enzymes that catalyze reactions in one direction can be easily reversed, and thus function in both pathways. A small number of steps utilize different enzymes in the forward versus the reverse direction. These enzymes are regulated in a coordinated fashion such that a pathway operates in only direction at time.

Pathways can be:

**Linear**

---

*A is the substrate for the first enzyme ( $E_1$ ) in the pathway, B is the product of the enzyme. The final product of the pathways is compound D. Note that this pathway can be reversed, using compound D to eventually synthesize compound A.*

### Branched

---

*An example of a branched pathway. The direction of the arrows indicate that this pathways is an anabolic, or synthetic, pathway where complex biomolecules D and F are synthesized using the simpler molecule A as starting material. In the reverse direction, the complex molecules D and F would be converted to A, releasing energy.*

### Circular

---

*In this circular pathway, compound A is transformed to compound B by the enzyme 1. A series of transformations eventually convert B back to A, restarting the cycle.*



Did I Get This?

## Introduction to Metabolism-Pathways

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 Regulation 

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# Introduction to Metabolism-Pathways

## Question 1

Metabolic pathways are usually reversible

Select one answer.

- A. Yes
- B. No

## Question 2

Metabolic pathways:

Select one answer.

- A. contain many intermediates.
- B. require the participation of a number of enzymes.
- C. are regulated.
- D. all of these answers are correct.

## Question 3

An anabolic pathway

Select one answer.

- A. consumes energy
- B. produce energy
- C. are branched
- D. produce electrons

Check your answers

^ Top ^

Close

# Regulation

[Hide](#)

## Learning Objectives

By the end of this module, students should be able to:

- Understand the major differences between a competitive and uncompetitive inhibitor.
- Understand activation of enzymes by allosteric compounds as a method of regulation.
- Understand regulation by non-covalent and covalent modification of enzymes.

It is essential that biochemical pathways are regulated, otherwise the cell would waste resources.

Some general properties associated with the regulation of metabolic pathways are listed below

- At least one step is regulated, often in multiple ways.
- Essentially irreversible steps, i.e. those with large energy changes, are regulated. Consequently, once the pathway is turned on, metabolites that enter the pathway are committed to complete the pathway.
- In synthetic and degradative pathways a common step is performed by different enzymes, each of which are regulated in a coordinated fashion such that only one pathway is on at a time.

There are five general methods by which the flux through a step in the pathway can be regulated.

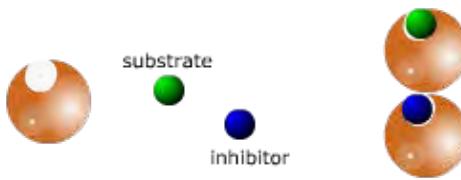
These methods differ in how rapidly they can respond to changes in the environment. Each of these methods is discussed below, with the more rapid form of regulation at the top of the list.

- Substrate availability.** For many enzymes, the intracellular level of substrate is below the level that half saturates the enzyme. Therefore, if the substrate concentration increases the rate of the reaction will increase due to the formation of additional enzyme-substrate complexes. If the substrate concentration is very low, the increase in the rate of the reaction is almost equal to the increase in substrate concentration.
- Product inhibition.** In this case the product of the reaction inhibits the enzyme that generated it, preventing the accumulation of intermediates in a pathway. The product is a competitive inhibitor of the enzyme that just created it.



Learn by Doing

## Using Inhibitors for Regulation



## Regulation

# Using Inhibitors for Regulation



Learn by Doing

## Effect of Inhibitors on Enzymes.

In this tutorial you will investigate the effect of competitive inhibitors on the steady-state kinetics of enzymes. From the nature of the changes in the kinetics, it is usually possible to distinguish one type of inhibitor from another. Product inhibition in metabolic pathways is one form of competitive inhibition, the product of an enzymatic reaction can usually bind to the active site where it was formed.

The tutorial is divided into two parts:

- 1) The first part will refresh your memory regarding how the rate of an enzyme catalyzed reaction depends on the concentration of substrate.
- 2) In the second part, you will explore how a competitive inhibitor binds to an enzyme and affects its kinetics.

As you work through this material, recall that the measured rate, or velocity, is proportional to [ES], the amount of enzyme substrate complex.

**Click the "Next" button to continue.**

Next

### Effect of Inhibitors on Enzymes.

Enzyme substrate binding with no inhibitors.

Hint

By what factor does the initial rate change when [S] is changed from 2 to 4?

- 1.5
- 2
- 0.5



## Effect of Inhibitors on Enzymes.

Competitive inhibitors.

Hint

The blue balls are binding to the enzymes using the same binding site that would be used by the substrate. The blue balls are **competitive** for the substrate binding site, and are therefore will be **competitive inhibitors**.

The black curve represents the velocity versus substrate obtained in the absence of any inhibitor.

Using the radio dials at the right, select substrate concentrations of  $[S]=2$  or  $[S]=4$ . The observed decrease in the velocity for the reaction in the presence of the inhibitor is lowered because:

- The amount of free enzyme is decreased, therefore the substrate has fewer places to bind, reducing  $[ES]$ .
- The substrate binds to the inhibitor in solution, reducing the concentration of substrate, therefore reducing the velocity.

Next



### Effect of Inhibitors on Enzymes.

Enzyme substrate binding with no inhibitors.

If you decreased the substrate concentration to 1, what would the best estimate for the reaction velocity?

Hint

- It would remain the same.
- It would be reduced to 50%.
- It would be reduced to 10%



Next

## Effect of Inhibitors on Enzymes.

Enzyme substrate binding with no inhibitors.

### Hint

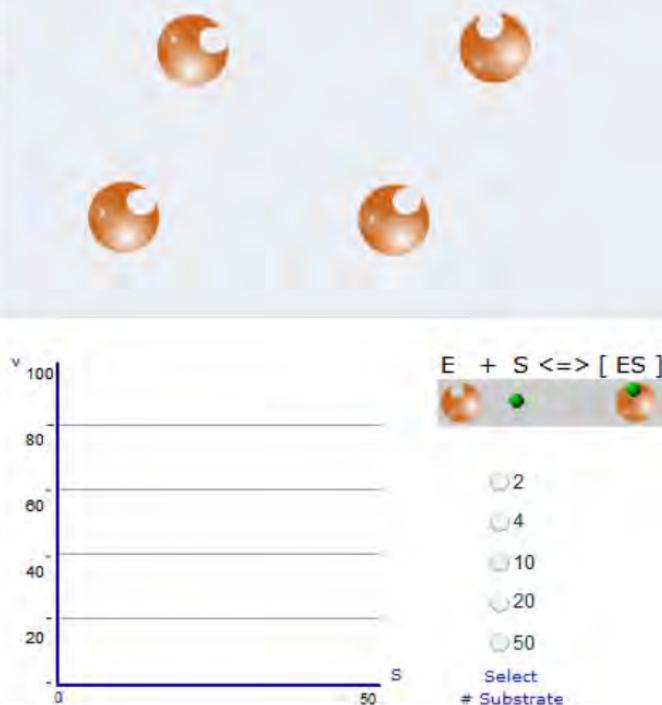
Now explore what happens at the high end of substrate concentrations.

Select [S]=20 and mentally note how frequently the enzymes have substrates bound and record the reaction velocity from the chart below.

If you increased the substrate to 50, what would you predict for the rate of the reaction:

- stay the same
- increase slightly
- increase proportionally, e.g. by 50/20

Next



## Effect of Inhibitors on Enzymes.

Enzyme substrate binding with no inhibitors.

### Hint

Which pair of equations best describes the relationship between [S] and the reaction velocity at low [S] and high [S], respectively.

- $v = k[S][S]$ ,  $v = k$ , i.e. initially quadratic, and then linear.
- $v = k[S][S]$ ,  $v = k$ , i.e. initially quadratic, and then independent of [S].
- $v = k[S]$ ,  $v = k$ , i.e. initially linear, and then independent of [S].



Next

### Effect of Inhibitors on Enzymes.

Enzyme substrate binding with no inhibitors.

#### Hint

Using the radio dials at the right, select increasing concentrations of substrate to investigate how the concentration of substrate affects the reaction velocity,  $v$ . The reaction velocity is just the rate of product formation/unit time, under steady-state conditions.

You can view the molecular events that occur in the upper animation and the velocity versus substrate is plotted on the lower graph.

Select  $[S]=2$ , and mentally note how frequently the four enzyme molecules have substrate. Now make  $[S]=4$ .

What happens to the average number of enzymes with substrate bound when  $[S]$  is increased from 2 to 4?

- increases
- decreases

Next





## Regulation

Would you expect the product of an enzyme catalyzed reaction function as a competitive or non-competitive inhibitor?

Did I Get This?

Submit and Compare



Did I Get This?

- **Feedback inhibitors.** In this case, a compound that is further down the pathway, or even a compound in a separate pathway, will inhibit a reaction. Again, this prevents an accumulation of intermediates in a pathway. The binding of the feedback inhibitor usually causes a change in the shape of the enzyme; a feedback inhibitor is an example of a non-competitive inhibitor or an allosteric inhibitor.

### Allosteric Pathway



Learn by Doing

### Allosteric Binding



Enzyme with  
substrate bound.



Enzyme with  
inhibitor bound.  
Substrate cannot  
bind.

- **Enzyme phosphorylation.** The addition of phosphate groups to serine, threonine, and tyrosine

# Allosteric Binding



Learn by Doing

## Allosteric Regulation of Enzymes.

In this tutorial you will investigate the effect of Allosteric regulators of enzyme activity.

Allosteric binding causes conformational changes in an enzyme that can either inhibit or activate the enzyme. In this example the conformation change is such that the substrate binding is affected.

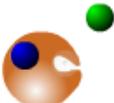
The substrate can not bind to the enzyme while the allosteric inhibitor is bound to the enzyme. This is an example of feedback inhibition.

The substrate can bind to the enzyme when the allosteric activator is bound.

Please click on the "Next" button to continue.



Enzyme with substrate bound.



Enzyme with inhibitor bound.  
Substrate cannot bind.

Next

residues on enzymes can cause a change in the shape of the active site of the enzyme. This change in shape is an allosteric effect. The change may lead to a more active enzyme (allosteric activator) or a less active enzyme (an allosteric inhibitor).

- **Enzyme levels.** Recall that the rate of product formation is proportional to the amount of enzyme. Enzyme levels can be increased by the conversion of inactive forms of the enzyme to active forms. This form of regulation occurs with digestive enzymes. These are made in an inactive form in the pancreas, but activated by cleavage in the small intestine. The levels of enzyme can also be varied by regulating the synthesis of the enzyme. This method of regulation is common during development, when certain enzymes are only present during defined developmental stages.



Did I Get This?

## Regulation of Metabolism

Before beginning the graded quiz below, provide the following response to the learning objectives for this topic.



My Response

## Metabolic Regulation



Quiz

## Pathways and Regulation

[^ Top ^](#) [Redox Reactions](#) 

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# Regulation of Metabolism

## Question 1

Which of the following enzymes are most likely to be regulated in the following pathway  
(select all that apply):

Select all that apply.

- A. E1
- B. E2
- C. E3
- D. E4
- E. E5
- F. E6

## Question 2

In the metabolic pathways shown below, which direction is anabolic, to the right or left?

Select one answer.

- A. Left
- B. Right

## Question 3

In the pathway shown below, compound G would act as a product inhibitor for enzyme \_\_\_\_\_ and a feedback inhibitor for enzyme \_\_\_\_\_.

Select one answer.

- A. E4, E1
- B. E6, E4
- C. E7, E4
- D. E4,E7

## Question 4

If the substrate concentration for an enzyme is doubled, the rate of the reaction

Select one answer.

- A. cannot be determined with this information.
- B. would double.
- C. would almost double.
- D. would stay the same.

## Question 5

Phosphorylation of enzymes always results in inhibition of activity.

Select one answer.

- A. True
- B. False

Check your answers

^ Top ^

Close

# Metabolic Regulation

Before leaving this topic, evaluate your ability to perform each of the following tasks.

Selecting 1 means "I could do this not at all", selecting 3 means "I could do this while relying on the course material" and selecting 5 means "I could do this perfectly on an exam."

	Not At All		With Support		On My Own
I can recognize, and describe, the major differences between a competitive and uncompetitive inhibitor. *					
I can recognize, and describe, the activation of enzymes by allosteric compounds as a method of regulation. *					
I can recognize, and describe, the regulation by non-covalent and covalent modification of enzymes. *					
	1	2	3	4	5

^ Top ^

# Pathways and Regulation

## Question 1

Many metabolic pathways involve multistep reactions. Consider the following pathway: A --E<sub>1</sub>--> B --E<sub>2</sub>--> C --E<sub>3</sub>--> D where A, B, C, and D are substrates and/or products of the three enzymes, E<sub>1</sub>, E<sub>2</sub>, E<sub>3</sub>. Feedback inhibition of this pathway is usually associated with

Select one answer.

10 points

- A. D interacting with an allosteric site on E<sub>1</sub>
- B. D interacting with an allosteric site on E<sub>2</sub>
- C. D interacting with an allosteric site in E<sub>3</sub>
- D. all of the intermediates or products in the reaction interacting with E<sub>1</sub>.

## Question 2

The fundamental difference between competitive and uncompetitive inhibition is

Select one answer.

10 points

- A. the size of the active site of the enzyme
- B. the manner of binding of the substrate to the enzyme
- C. the manner of binding of the inhibitor to the enzyme

## Question 3

When substrate levels are very high (saturating) the presence of the following inhibitor type will not affect the maximal velocity ( $V_{max}$ ).

Select one answer.

10 points

- A. competitive inhibition
- B. uncompetitive inhibition
- C. both forms of inhibition

## Question 4

In allosteric interactions

Select one answer.

10 points

- A. proteins that consist of a single polypeptide chain form aggregates
- B. disulfide bonds are broken
- C. changes that take place in one site of a protein cause functionally important changes at a distant site
- D. metal ions always bind to the protein

## Question 5

An allosteric activator is similar to a competitive inhibitor because it binds to the active site of an enzyme, increasing the catalytic rate.

Select one answer.  
*10 points*

- A. False
- B. True

## Question 6

Both allosteric activators and activation of enzymes by phosphorylation involve non-covalent binding of the activator to the enzyme.

Select one answer.  
*10 points*

- A. False
- B. True

## Question 7

Protein phosphorylation

Select one answer.  
*10 points*

- A. plays no role in the regulation of enzyme activity.
- B. plays a role in the regulation of the activity of a number of enzymes.
- C. usually involves the addition of phosphates to Cys residues.
- D. occurs spontaneously when proteins are incubated in phosphate buffer.

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Save      Submit and finish

# Redox Reactions

[Hide](#)

## Learning Objectives

By the end of this module, students should be able to:

- Understand the direction of electron transfer in oxidation/reduction reactions.
- State the name of two common organic electron carriers and show familiarity with changes in the structure that occurs on oxidation/reduction.
- Learn how to balance redox reactions.

Oxidation-reduction reactions, or **Redox** reactions are common in metabolic pathways. Generally, degradative (catabolic) pathways cause the net oxidation of compounds, releasing energy. In contrast, synthetic (anabolic) pathways, are generally reductive pathways.

**Oxidations** involve the loss of electrons.

**Reductions** involve the gain of electrons.

Here are two mnemonics to help you remember where the electrons go during redox reactions:

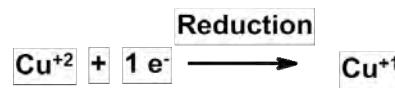
- LEO GER:** "leo [the lion] goes grr". Lose electrons oxidation, gain electron reduction.
- OIL RIG:** Oxidation involves loss, reduction involves gain.

An example of an oxidation is the conversion of iron from its metallic state,  $\text{Fe}^0$ , to its rusted form,  $\text{Fe}^{+3}$ , by the loss of three electrons.



*Oxidation and reduction of iron. Metallic iron,  $\text{Fe}^0$ , becomes oxidized to  $\text{Fe}^{+3}$  (otherwise known as rust) by the removal of 3 electrons.*

The above reaction is an incomplete description of a redox reaction because it does not indicate the fate of the electrons that were obtained from iron. Since free electrons generally cannot exist, all oxidation reactions must be coupled to a corresponding reduction. Since the above reaction only describes one-half of the reaction it is referred to as a **half-reaction**. The oxidation of iron could be coupled to the reduction of copper ions, which is described by the following half-reaction:



*Reduction of copper ion from its +2 state to +1 state by gain of an electron.*

The complete reaction, balanced such that there are no free electrons, is:

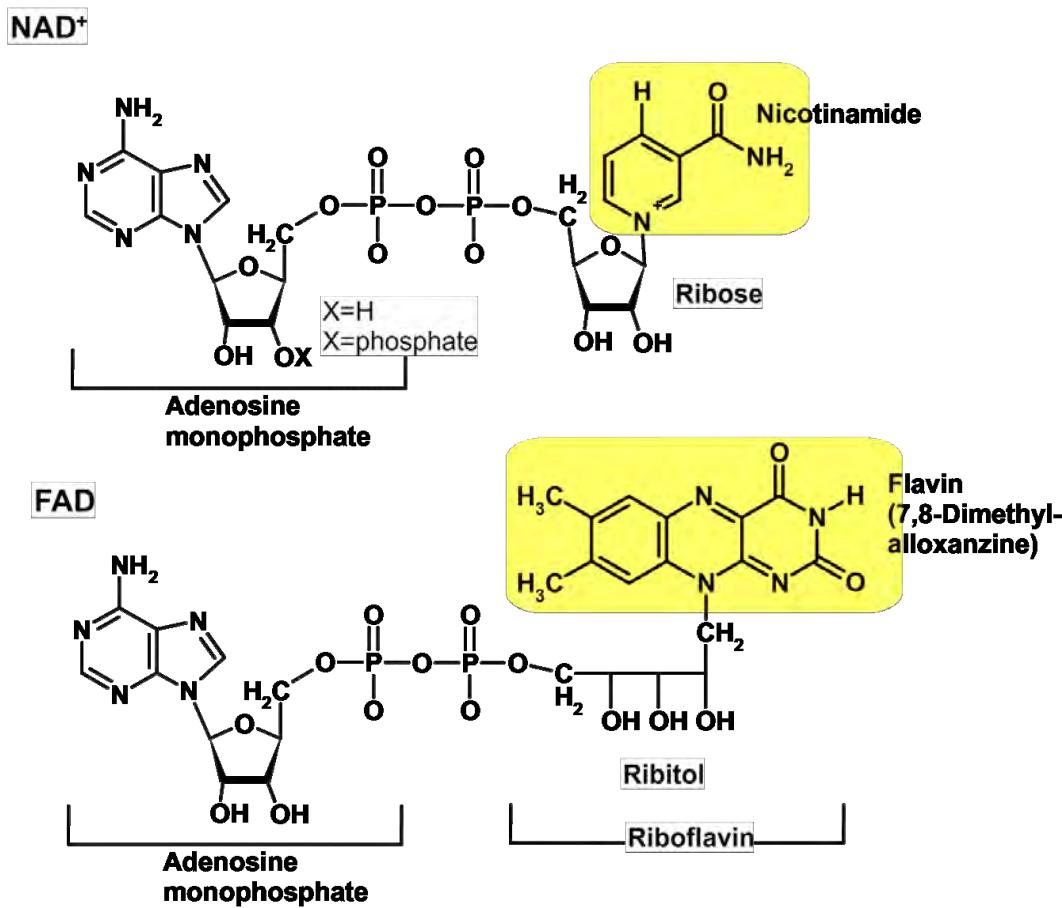


*A balanced redox equation. Three copper<sup>+2</sup> ions provide a total of three electrons to oxidize metallic iron to  $\text{Fe}^{+3}$ . Note that there are no free electrons.*

The pair of compounds that exchange electrons are often referred to as a **redox couple**.

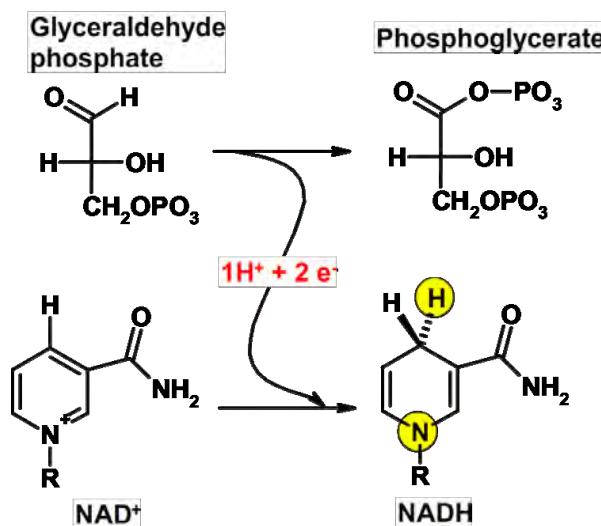
## Redox Carriers

In most biochemical redox reactions a total of two electrons are transferred. These electrons are often transferred as hydrogen atoms, containing a proton and electron. Two common electron acceptors are NAD<sup>+</sup> (nicotinamide adenine dinucleotide) and FAD (flavin adenine dinucleotide). They both can accept two electrons, giving the reduced forms NADH and FADH<sub>2</sub>, respectively. The structure of the oxidized forms of these compounds are shown below.



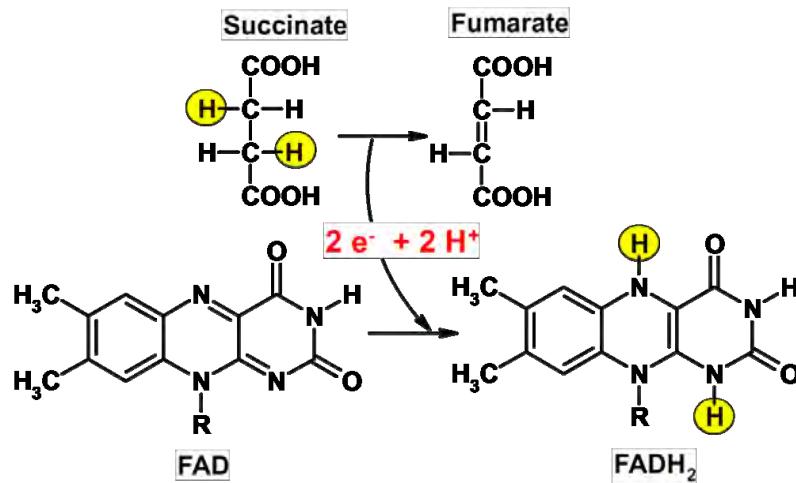
The chemical structures of nicotinamide adenine dinucleotide (NAD<sup>+</sup>) and flavin adenine dinucleotide (FAD) are shown. These two compounds are commonly used as electron acceptors in metabolic pathways. The portion of each molecule that accepts electrons during the reduction process is highlighted in yellow.

**Oxidation of NAD<sup>+</sup>.** In the oxidation of glyceraldehyde to phosphoglycerate an aldehyde is oxidized to a carboxylic acid and the released electrons are placed on to NAD<sup>+</sup> to form NADH.



The oxidation of an aldehyde to a carboxylic acid. The two electrons released by the aldehyde are transferred to  $\text{NAD}^+$  to make  $\text{NADH}$ . In this diagram only the portion of  $\text{NAD}^+/\text{NADH}$  that undergoes chemical changes is shown. The remaining part of the  $\text{NAD}$  molecule is represented by ' $\text{R}$ '.

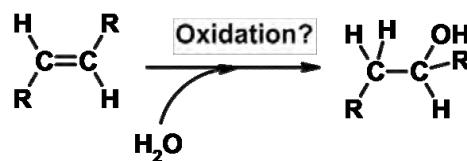
**Oxidation of FAD.** The oxidation of succinate to fumarate, using FAD as an electron acceptor is another example of a redox reaction found in a metabolic pathway. Two hydrogen atoms (= two electron plus two protons) are removed from succinate and placed on FAD, producing fumarate and  $\text{FADH}_2$ , oxidizing a carbon-carbon single bond to a double bond.



The oxidation of an alkane to an alkene. The two electrons released by the alkane are transferred to  $\text{FAD}$  to make  $\text{FADH}_2$ . In this diagram only the portion of  $\text{FAD/FADH}_2$  that undergoes chemical changes is shown. The remaining part of the  $\text{FAD}$  molecule is represented by ' $\text{R}$ '.

## Balancing Redox Reactions

It is often difficult to determine from the structure of an organic compound whether it has been oxidized or reduced in a reaction. For example, the addition of a water molecule to an double bond (alkene) appears to be a redox reaction because an -OH group has been added .



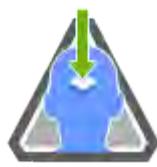
*The addition of water to a double bond is a common reaction in many pathways. Is it a redox reaction?*

The rules for balancing redox reactions are as follows:

1. Make the number of oxygen atoms in the reactant and product equal by adding the appropriate number of water molecules to one side of the reaction or the other.
2. Use  $\text{H}^+$ , or  $\text{H}^+ + \text{e}^-$ , or  $\text{e}^-$  to balance hydrogen atoms and/or charge.
3. A redox reaction has occurred if electrons are consumed or released

The above reaction is balanced as is, and is therefore not a redox reaction.

Try the following mini-tutor to test your skill at assessing whether a redox reaction has occurred.



## Redox Reactions

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Energy Storage in Metabolism

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# Redox Reactions

## Question 1

When a molecule participates in a redox reaction, which of the following properties of the molecule change?

Select one answer.

- A. The number of phosphate groups.
- B. The number of electrons.
- C. The size of the molecule, by cleavage into two parts.
- D. A double bond is converted to an alcohol, by the addition of oxygen from water.

## Question 2

Oxidation of a compound involves the \_\_\_\_\_ and generally \_\_\_\_\_.

Select one answer.

- A. gain of electrons, releases energy.
- B. gain of electrons, consumes energy.
- C. loss of electrons, releases energy.
- D. loss of electrons, consumes energy.

## Question 3

When a compound is oxidized, which of the following also occur.

Select one answer.

- A. nothing else occurs.
- B. another compound is reduced.
- C. the energy of the system decreases substantially.

## Question 4

Which of the following molecules is used by a cell to carry energy in the form of electrons from one pathway to another (select all that apply)

Select all that apply.

- A. sugar (glucose)
- B. fats (triglycerides)

- C. NADH
- D. NAD<sup>+</sup>
- E. FADH<sub>2</sub>
- F. ATP
- G. FAD

## Question 5

The compounds like the ones shown below occur in the TCA cycle and in fatty acid oxidation. Given that these pathways are oxidative, what order do these compounds appear in the pathway?

Select one answer.

-  [?]
- A. A, B, C, D
  - B. B, A, D, C
  - C. C, D, A, B
  - D. B, A, C, D

Check your answers

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# Energy Storage in Metabolism

Hide

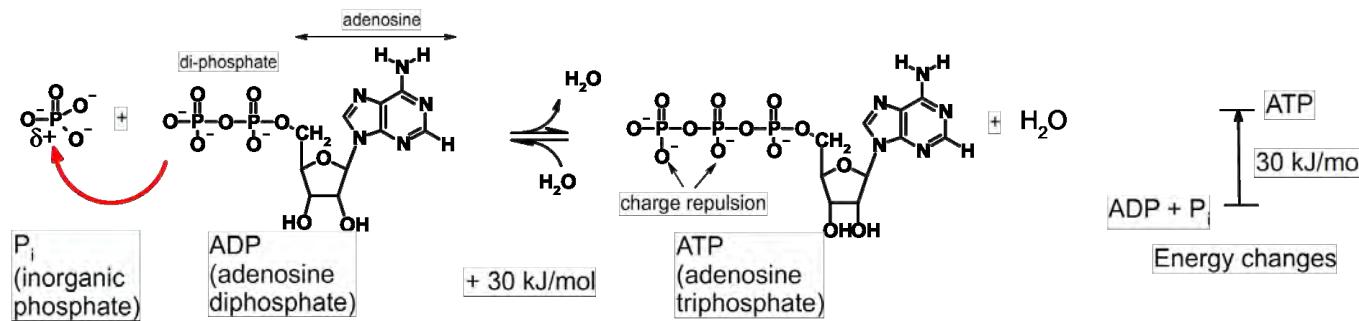
## Learning Objectives

By the end of this module, students should be able to:

- Understand the major energy storage methods in metabolism - phosphorylated compounds, redox carriers, proton gradient.
- Understand the source of "high-energy" phosphate bonds in ATP
- How the energy stored in a thioester can be used for ATP synthesis or organic addition reactions.

The operation of a metabolic pathway produces (catabolic) or consumes (anabolic) energy. There are a number of different forms of energy storage that are found in metabolic pathways. These include:

- Phosphorylated Compounds** Nucleoside triphosphates, such as adenosine triphosphate (ATP) are commonly used to store energy. The addition of an inorganic phosphate group to a nucleotide diphosphate to form the triphosphate requires approximately 30 kJ/mol of energy. The reaction showing the synthesis of ATP from ADP and phosphate is pictured below.



Phosphorylation of adenosine diphosphate (ADP) produces adenosine triphosphate (ATP). This reaction requires the input of approximately 30 kJ/mol. Formation of ATP occurs when the negatively charged phosphate group on ADP attacks the electropositive phosphate in inorganic phosphate, forming a phosphate anhydride bond with the release of water (red arrow).

ATP can be used to phosphorylate other nucleoside diphosphates with essentially no input of energy, for example:

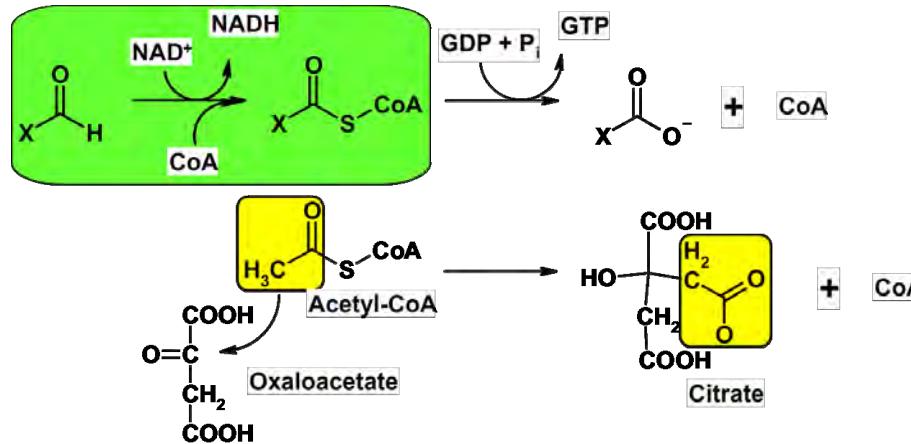


**The myth of high-energy phosphate bonds.** When a phosphate is released from ATP to form ADP, about 30 kJ/mol of energy is released. It is often stated, incorrectly, that the bond that is broken is "high-energy". In fact, its energy is no different than any other phosphate bond of the same type. The release of energy is due to the fact that the products, ADP and inorganic phosphate, are lower in energy than ATP by 30 kJ/mol. One reason that ATP is higher in energy is due to charge repulsion between the negatively charged phosphate groups. Once the phosphate group is removed, the unfavorable repulsion disappears.

- Reduced redox carriers.** The oxidation of metabolites usually produces energy. If this energy was not captured in some way, it would be lost as heat. The reduced form of redox carriers, such as NADH and FADH<sub>2</sub>, are higher in energy than their corresponding oxidized forms,

capturing the energy that would otherwise be lost as heat. For example, the oxidation of isocitrate to ketoglutarate releases approximately 70 kJ/mol, 60 of which is captured by converting NAD<sup>+</sup> to NADH.

3. **High energy thioesters** are often produced by oxidative steps. For example, the energy released by the oxidation of an aldehyde is stored in both the reduced form of NAD<sup>+</sup> as well in a thioester. The hydrolysis of the thioester can be used to synthesize nucleoside triphosphates or to facilitate the formation of carbon-carbon bonds, as shown below.



The oxidation of the aldehyde to the thioester is highlighted in green. CoA is coenzyme A, a nucleotide containing cofactor that is an essential co-substrate for many reactions. Part of the energy of this oxidation, 60 kJ/mol, is captured by the formation of NADH. The energy stored in the thioester can be used to either phosphorylate GDP to form GTP, capturing another 30 kJ/mol. In the case of acetyl-CoA (lower diagram) the thioester facilitates the attachment of the acetyl group to oxaloacetate to form citrate, the first compound in the TCA cycle.

4. **Proton gradient** The transfer of electrons from NADH and FADH<sub>2</sub> to oxygen to form water during the electron transport chain, provides energy for the pumping of protons across the inner mitochondrial membrane. This is equivalent to pumping water up hill to fill a reservoir. As the protons flow back through the membrane, the energy released is used to generate ATP, in much the same way water generates electricity in a hydroelectric plant.



## Metabolism Energy

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# Metabolism Energy

## Question 1

The products of ATP hydrolysis, ADP and inorganic phosphate, are more stable because | Select one answer.

- A. The bond that is broken is higher in energy than other phosphate-phosphate bonds.
- B. Electrostatic repulsion between the phosphates is relieved.
- C. Additional hydrogen bonds can be formed to the new phosphate.

## Question 2

ATP is an important molecule in metabolism because: | Select one answer.

- A. It is very stable.
- B. It can be used as an energy source in many reactions.
- C. It participates in redox reactions, storing the energy from oxidations.

## Question 3

Which of the following molecules is used by a cell to carry energy in the form of electrons? | Select one answer.

- A. ATP
- B. NAD<sup>+</sup>
- C. Oxidized compounds.
- D. Thioesters.

## Question 4

The energy from electrons on electron carriers is used to directly form | Select one answer.

- A. ATP
- B. A proton gradient
- C. High energy thioesters.

# Thermodynamics

Hide

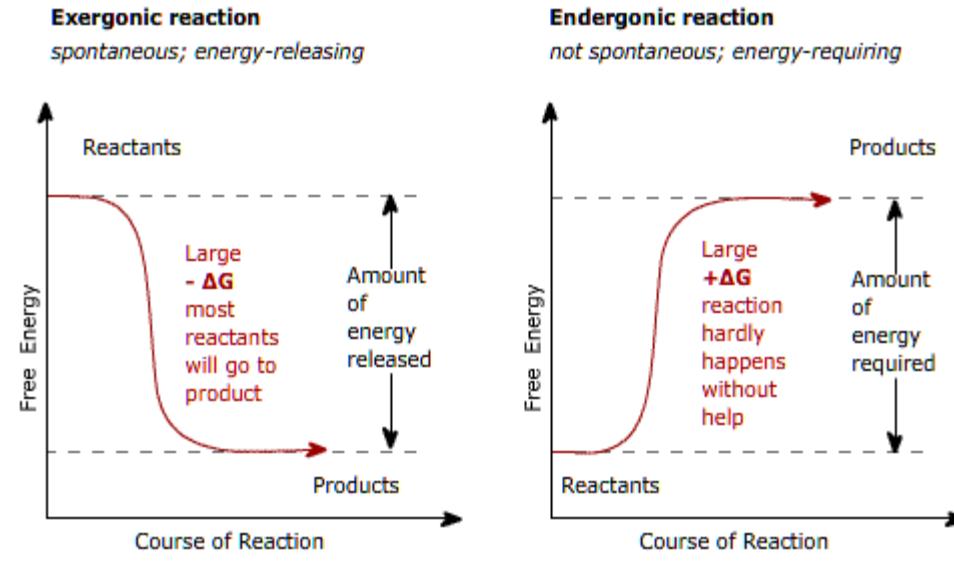
## Learning Objectives

By the end of this module, students should be able to:

- Understand the difference between standard energy and Gibbs free energy.
- Understand the relationship between the equilibrium point of a system and the difference in standard energies.
- Calculate the Gibbs free energy change, given the state of the system and the standard energy changes.
- Determine the spontaneous direction of a reaction from the Gibbs free energy.

## Free Energy and Spontaneity

Pathways accomplish the net conversion of the starting compounds to the final product of the pathway. During the normal operation of a pathway there is a constant flux of material through the pathway in one direction. Note that many pathways are reversible and operate in the forward or reverse direction, depending on the needs of the organism. The direction of a pathway depends on the energy difference between the starting compounds and final product of the pathway. The pathway will be spontaneous in the direction that causes a decrease in the **free energy** of the system. Reversing the direction of a pathway requires changing the relative energies of the reactants and products



It is useful to have a quantitative way to predict the direction of a pathway given the current environment in the cell. A method of predicting the direction of a reaction was devised by J. Willard Gibbs in 1876 and the quantitative parameter that can be used to predict the direction of a reaction is called the **Gibbs free energy**. This method is particularly useful because it can be applied to reactions that are not at equilibrium, which is the situation encountered during metabolism. Before

we can discuss the Gibbs free energy, we have to discuss standard energies and their relationship to equilibrium positions of reactions. Keep in mind that these discussions relate to the **thermodynamic** properties of pathways, more specifically the relative energy differences between reactants and products under cellular conditions. The presence of enzymes simply increases the rate of conversion from reactants to products, the enzyme cannot alter the relative energies of these compounds.

---

## Equilibria

Consider the simple reaction [A] to [B]. If we start with a system that is pure [A] it will spontaneously form some [B] until equilibrium is reached. When a system is at equilibrium, the concentration of products and reactants are constant and it is possible to write an equilibrium constant for the reaction:

where,  $K_{EQ}$  is:

$$K_{EQ} = [B] / [A]$$

Note that [A] and [B] are at their **equilibrium** concentrations in this formula.

---

## Standard Energy

The standard energy change is the energy change when one mole of reactant is converted to one mole of product, it is the energy difference between reactants and products:  $\Delta G^{\circ} = G_{products}^{\circ} - G_{reactants}^{\circ}$ . The standard energy change defines the equilibrium position of a reaction through the following equation:

$$\Delta G^{\circ} = -RT \ln K_{EQ} \quad \text{or} \quad K_{EQ} = e^{-\Delta G^{\circ} / RT}$$

For the simple reaction of A to B, the fraction of the system in state [A] is:

$$f_A = [A] / ([A] + [B]) = 1 / (1 + K_{EQ})$$

In a similar fashion, the fraction in state [B] is:

$$f_B = [B] / ([A] + [B]) = K_{EQ} / (1 + K_{EQ})$$

You can see from the above equations that if the energy of the products are equal to the reactants, then the equilibrium concentration of [B] will be equal to [A]. Mathematically, this can be shown as follows:

If the energy of [B] is equal to [A], then  $\Delta G^{\circ} = 0$ . Therefore

$K_{EQ}=1$ , and

$$f_A=1/(1+1) = 0.5 \text{ and } f_B=1/(1+1) = 0.5$$

---

**Question:** What will happen to the relative concentrations of A and B if the energy of form A is

lower than B, what will happen if the energy of form A is higher? Use the Learn-by-Doing tutorial below to find out.

---



---

## Gibbs Free Energy

The formula for change in the Gibbs free energy in the reaction for the reaction direction [A] to [B] is:

$$\Delta G = \Delta G_0 + RT\ln [ B ] / [ A ]$$

Note that in this equation, the concentration of [A] and [B] are not necessarily at their equilibrium concentrations.

It can be shown that:

- If  $\Delta G < 0$  then the reaction is not at equilibrium and will proceed spontaneously in the forward direction, A to B.
- If  $\Delta G > 0$  then the reaction is also not at equilibrium, but will proceed spontaneously in the reverse direction, B to A.
- If  $\Delta G = 0$  the reaction is at equilibrium and the concentrations of reactants and products will not change.

You can explore these relationships in the following tutorial.

In addition to predicting the direction of the reaction, the absolute value of  $\Delta G$ ,  $| \Delta G |$ , is the amount of energy released when the concentrations of reactants and products change from their non-equilibrium values to their equilibrium values.

**Question:** What is the Gibbs free energy when the concentration of A is greater than its equilibrium value? In what direction will the reaction flow? From A to B or from B to A? Use the Learn-by-Doing tutorial below to find out.

---



Learn by Doing

### Calculating Free Energy



Did I Get This?

### Thermodynamics



Before leaving this page, provide the following response to the learning objectives for this topic.

### Thermodynamics

# Calculating Free Energy



Learn by Doing

Equilibrium position of a reaction defined by standard energy change,  $\Delta G^\circ$

The upper part of the right window shows 20 molecules that can be either in form A or form B. These two forms are in equilibrium with each other and will interconvert randomly.

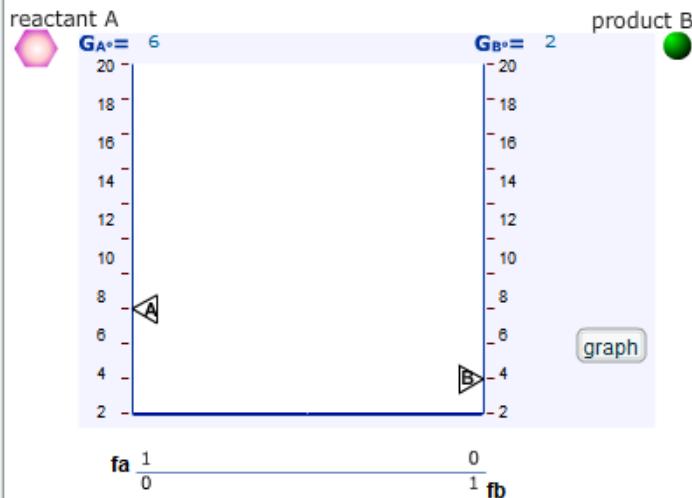


The lower part of the right window shows a quantitative representation of the equilibrium position and Gibbs free energy of the system.

The scales underneath the graph indicate the fraction of the molecules in form A (upper) and form B (lower). The extreme left represents a system where all of the molecules are in form A and the extreme right represents a system where all of the molecules are in form B.

You can select the standard energy of each reactant by using the sliders labeled A and B. The numerical values you select appear at the top of the column.

Click "Next" to continue.



Next

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# Thermodynamics

## Question 1

A reaction will be spontaneous in the reverse direction if the standard energy change is positive.

Select one answer.

- A. true
- B. false

## Question 2

The direction in which a reaction is spontaneous is controlled by all of the following EXCEPT

Select one answer.

- A. concentration of reactants
- B. concentration of products
- C. a catalyst
- D. standard energy changes

## Question 3

For the conversion of compound A to compound B to be spontaneous in the direction of A to B, the following will be true

Select one answer.

- A. The concentration of A will be greater than its equilibrium value..
- B. the standard free energy change will be negative.
- C. an enzyme will be provided to catalyze the reaction.
- D. the Gibbs free energy change will be negative.

## Question 4

If the standard energy change for converting [A] to [B] is zero, then the reaction will be spontaneous in the direction [A] to [B] under the following conditions (select all that apply).

Select one answer.

- A. When the concentration of [A] equals [B].
- B. When the concentration of [A] is higher than its equilibrium value.

- C. When the concentration of [A] is lower than its equilibrium value
- D. When the concentration of [B] is lower than its equilibrium value.
- E. When the concentration of [B] is higher than its equilibrium value.

Check your answers

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# Thermodynamics

Before leaving this topic, evaluate your ability to perform each of the following tasks.

Selecting 1 means "I could do this not at all", selecting 3 means "I could do this while relying on the course material" and selecting 5 means "I could do this perfectly on an exam."

	Not At All		With Support		On My Own
I can recognize, and describe, the difference between standard energy and Gibbs free energy. *					
I can recognize, and describe, the relationship between the equilibrium point of a system and the difference in standard energies. *					
I can calculate the Gibbs free energy change, given the state of the system and the standard energy changes. *					
I can determine the spontaneous direction of a reaction from the Gibbs free energy. *					
	1	2	3	4	5

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# Coupling in Metabolism

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## Learning Objectives

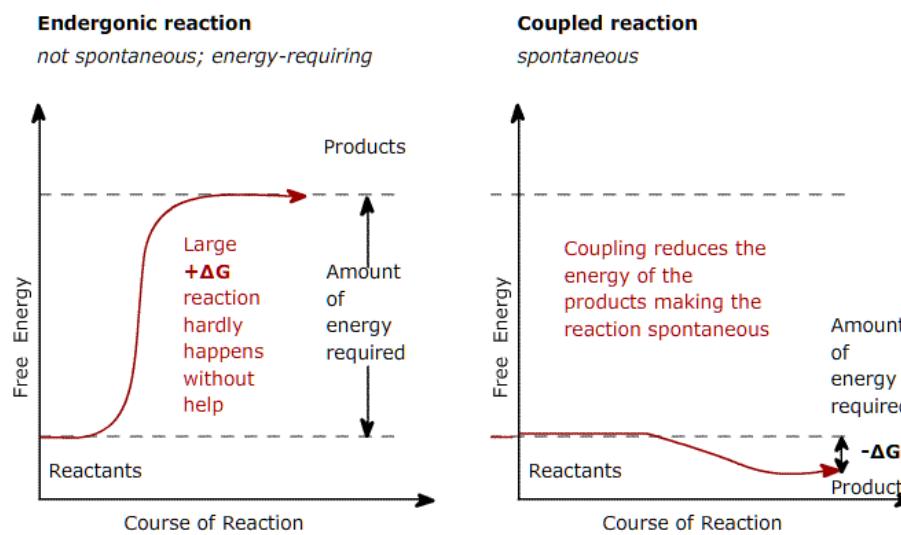
By the end of this module, students should be able to:

- Understand how a pathway with a positive Gibbs free energy can be reversed by coupling to an energy releasing reaction.
- Understand the difference between direct and indirect coupling.

A reaction will be spontaneous in the forward direction if the Gibbs free energy for that reaction is less than zero. The same reaction, if run in the reverse direction, will have a positive Gibbs free energy and will therefore be non-spontaneous. If it is necessary to reverse the direction of this reaction to reverse the direction of the pathway, then the sign of the Gibbs free energy for the reverse reaction has to become negative. If you recall, the Gibbs free energy:

$$\Delta G = \Delta G^0 + RT\ln [B][A]$$

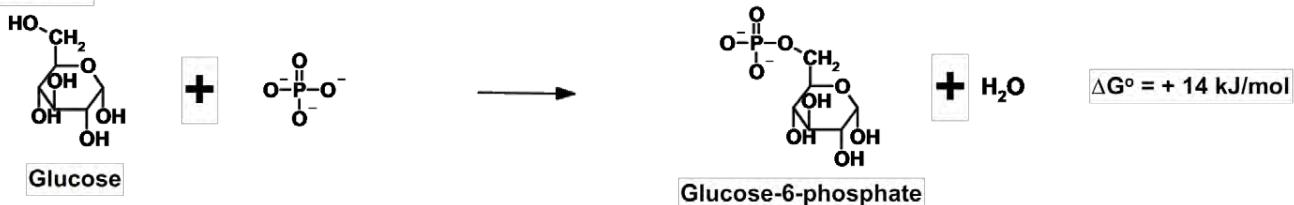
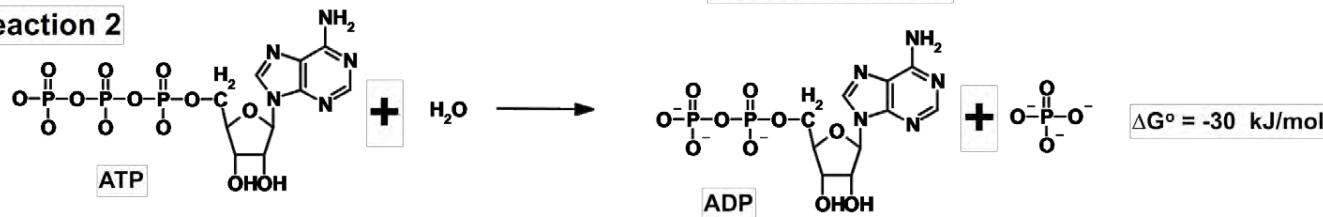
consists of two parts, the standard energy change,  $\Delta G^0$ , and a term that accounts for the non-equilibrium concentrations of [A] and [B]. Consequently, an unfavorable reaction with a positive Gibbs free energy can be made spontaneous by making the sum of these two terms negative by coupling the unfavorable reaction to a favorable, energy releasing one. The energy releasing reaction provides the necessary energy to change the sign of the Gibbs free energy from positive to negative.



There are two forms of coupling, both may be used to ensure a negative Gibbs free energy, direct and indirect coupling. Direct coupling reduces the standard free energy while indirect coupling reduces the second term of the equation. Both of these methods are described in more detail below.

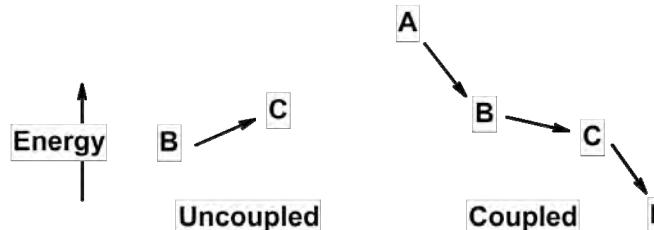
- Direct coupling** In this case a large negative  $\Delta G^0$  for the reaction is created by directly coupling the unfavorable reaction to a favorable one on the same enzyme. For example, the phosphorylation of glucose is very unfavorable if inorganic phosphate is used as the source of phosphate. The standard energy change of +14 kJ/mol makes the Gibbs energy positive. However, if the unfavorable reaction is coupled to the conversion of ATP to ADP within the active

site of the enzyme hexose kinase the 30 kJ of energy released from ATP can be utilized to reduce the standard energy change such that the overall Gibbs free energy becomes negative. The overall reaction is the transfer of phosphate from ATP to glucose, with an overall standard energy change of approximately -15 kJ/mol.

**Reaction 1****Reaction 2****Sum**

*Direct coupling:* Reaction 1 and 2 are hypothetical half-reactions that sum to give the complete reaction at the bottom of the image. In the actual reaction the enzyme glucose kinase transfers the phosphate group directly from ATP to glucose; hydrolysis of the ATP does not occur. Note that the two half-reactions sum to give the complete reaction, both in terms of the compounds involved as well as the overall standard energy change.

2. **Indirect coupling.** The Gibbs free energy can also become negative by either having a favorable reaction that precedes the unfavorable one, or a favorable reaction that follows the unfavorable one. In the first case, the favorable preceding reaction causes the concentration of the substrates for the following unfavorable reaction to be higher than equilibrium, making  $\Delta G$  negative. For the case of a favorable following reaction, the concentration of the products of the unfavorable reaction are kept to a level that is smaller than the equilibrium concentration, again making  $\Delta G$  negative. This type of coupling between reactions is referred to as indirect coupling because the coupling between favorable and unfavorable reactions occurs indirectly, via alteration of concentrations of reactants and products.



*Indirect coupling:* In the absence of coupling (left) the conversion of [B] to [C] is uphill energetically, and therefore not favorable. If the preceding step ([A] to [B]) is very favorable, the concentration of [B] increases to a level above its equilibrium level, which decreases the Gibbs free energy for step [B] to [C]. Alternatively, if the following step ([C] to [D]) is favorable, the concentration of [C] will be lower than its equilibrium level, which also decreases the Gibbs free energy for the step [B] to [C].

**Coupling**

The following quiz will be graded and recorded in the grade book. You may take this quiz only once.



Quiz

## Metabolism - Energetics

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Enzyme Nomenclature



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# Coupling

## Question 1

The reaction that converts A to B in a cell is nonspontaneous under standard conditions. One means of overcoming this nonspontaneous reaction in the cell is to increase the amount of B and decrease the amount of A.

Select one answer.

- A. True
- B. False

## Question 2

The covalent bonding of a phosphate to molecule X to form X-P is a nonspontaneous process with a standard free energy ( $G^{\circ}$ ) change of +10 kJ/mole. This reaction can be coupled to the hydrolysis of ATP with its free energy change of -30 kJ/mole. The result is:

Select one answer.

- A. The spontaneous breakdown of X-P with a free energy change of -20 kJ/mole
- B. the spontaneous phosphorylation of X with a standard free energy change of -20kJ/mole
- C. The spontaneous phosphorylation of X with a total standard energy change of -40 kJ/mole
- D. The spontaneous phosphorylation of ADP with a total standard energy change of -20 kJ/mole

## Question 3

The Gibbs free energy for a reaction can become negative by:

Select one answer.

- A. reducing the standard free energy,  $G^{\circ}$ .
- B. Making the concentration of the products lower than their equilibrium concentration.
- C. Making the concentration of the reactants higher than their equilibrium concentration.
- D. all of these are correct.

Check your answers

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Close

# Metabolism - Energetics

## Question 1

Which of the following is not a redox reaction? 

- A. A
- B. B
- C. C
- D. D

Select one answer.

10 points

## Question 2

The term "high-energy bond" refers to

- A. one for which hydrolysis releases a useful amount of energy.
- B. one that cannot be broken below 80C.
- C. a bond that requires the input of at least 100 kJ/mol to break.

Select one answer.

10 points

## Question 3

The hydrolysis of ATP can be used to drive reactions that have a  $\Delta G^\circ$  that is

- A. less than +30.5 kJ/mol.
- B. greater than +30.5 kJ/mol.
- C. between +20 and +40 kJ/mol.
- D. not possible to determine from the information given.

Select one answer.

10 points

## Question 4

The hydrolysis of a thioester releases as much energy as the hydrolysis of (pick the closest answer):

- A. Phosphoenolpyruvate

Select one answer.

10 points

- B.** ATP
- C.** Glucose-6-phosphate

## Question 5

Order the following chemicals from lowest oxidation level to highest oxidation level.

Ethane, CH<sub>3</sub>-CH<sub>3</sub>.

Formic Acid, CH<sub>3</sub>-CHOOH.

Acetaldehyde, CH<sub>3</sub>-CH<sub>2</sub>=O.

Ethanol, CH<sub>3</sub>-CH<sub>2</sub>-OH.

Click and drag each box to order them. Tab: Select next item. Shift+Tab: Select previous item. Arrow Down: Move item down. Arrow Up: Move item up.

10 points

## Question 6

Which of the following electron carriers is usually tightly bound to enzymes?

- A.** ATP
- B.** NAD
- C.** FAD
- D.** Pyruvate

Select one answer.

10 points

## Question 7

If the standard energy difference between A and B is +10 kJ/mole then

- A.** At equilibrium [A] is less than [B]
- B.** At equilibrium [A] equals [B].
- C.** At equilibrium [A] is greater than [B].
- D.** No conclusions can be drawn unless the Gibbs energy is known.

Select one answer.

10 points

## Question 8

If the Gibbs energy difference between A and B is -10 kJ/mole then

Select one answer.

10 points

- A. The reaction will spontaneously go from A to B.
- B. The reaction is at equilibrium, and [A] is greater than [B]
- C. The reaction will spontaneously go from B to A.,
- D. No conclusions can be drawn unless the standard energy is known.

## Question 9

The phenomenon of coupling always involves

Select one answer.

10 points

- A. reactions that produce energy and reactions that consume energy.
- B. oxidation and reduction reactions.
- C. decarboxylation reactions.
- D. esterification reactions.

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# Enzyme Nomenclature

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## Learning Objectives

By the end of this module, students should be able to:

- Understand the difference between a kinase and a phosphatase
- Understand the reactions catalyzed by dehydrogenases, hydratases, isomerases, and synthetases.

There are thousands of different enzymes in any cell. Most enzymes bind a specific substrate, perform a simple chemical change on that substrate, and then release a product.

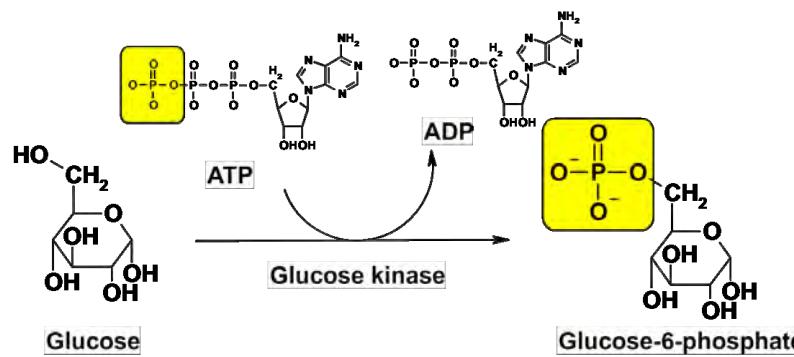
Each enzyme has a unique name. Usually, the name of an enzymes is systematic, but many exceptions exist. Almost all enzyme names have the suffix **ase**, indicating that they are an enzyme, for example **kinase**, **lyase**, **phosphatase**, etc. Usually, but unfortunately not always, the name of the enzyme is derived from the nature of the chemical change that it catalyzes. For example, an enzyme that oxidizes its substrate is referred to as a dehydrogenase because it removes hydrogens atoms during the oxidation process.

To further clarify the name of the enzyme, the name of the substrate or product is often included in the name. For example, the enzyme that oxidizes succinate is called succinate dehydrogenase. Keep in mind that most reactions in pathways are reversible, so the name may describe the reverse reaction. Lastly, in cases when enzymes bind more than one substrate, the name can also suggest the co-substrate. For examples, dehydrogenases will use  $\text{NAD}^+$  or FAD as co-substrates.

## Important Classes of enzymes

Although there is a large number of enzyme catalyzed reactions in a cell, the following list describes most of the activities that are found in metabolic pathways.

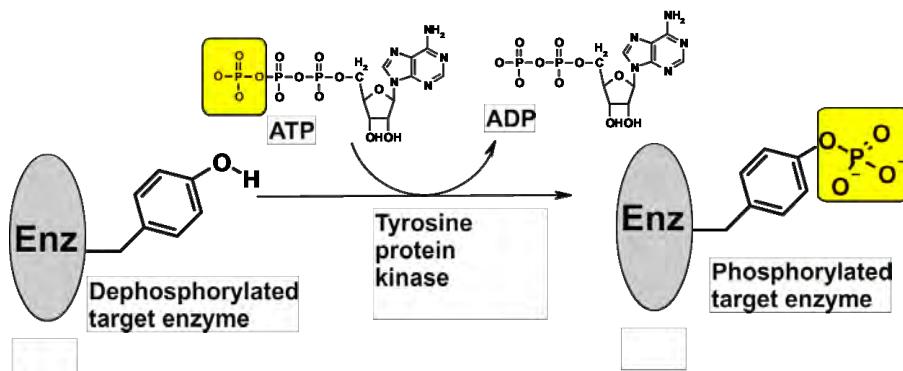
**Kinase.** A kinase transfers a phosphate group from ATP to the substrate. Kinases are used when direct coupling is required to reduce the Gibbs free energy of the reaction.



*Phosphorylation of glucose by glucose kinase. Note that the source of phosphate is ATP, not inorganic phosphate.*

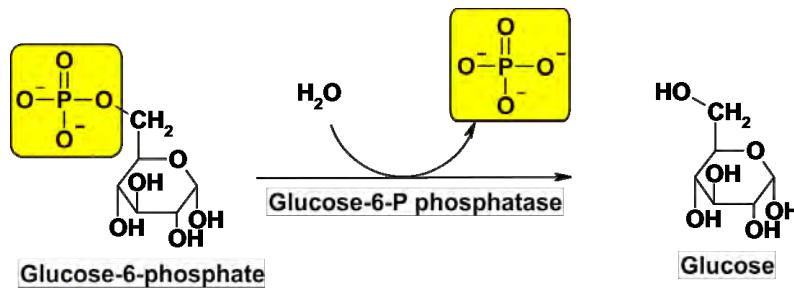
Alternatively, a kinase may be involved in regulation of enzymes by transferring a phosphate from

ATP to a Serine, Threonine, or Tyrosine on the enzyme that is being regulated. The phosphorylated form of the enzyme may be active or inactive.



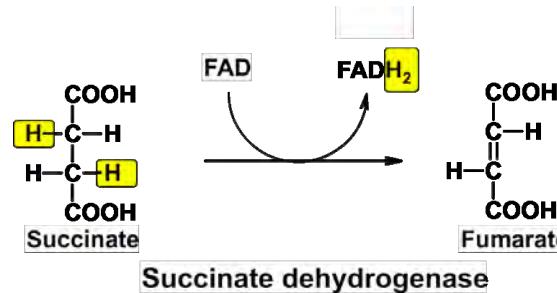
*A protein kinase phosphorylates an enzyme, causing it to change its state from active to inactive or from inactive to active.*

**Phosphatase.** A phosphatase removes a phosphate group by a hydrolysis reaction, producing inorganic phosphate. ADP or ATP are not involved in the reaction.



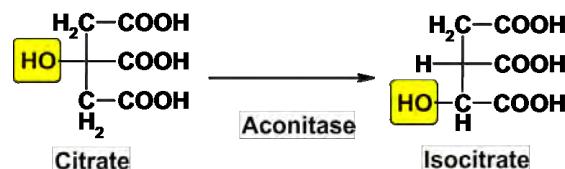
*A phosphatase uses water to remove a phosphate group from its substrate. Phosphatases can act on small molecules, as shown above, or on phosphorylated proteins.*

**Dehydrogenase.** As the name suggests, enzymes of this group transfer hydrogen atoms from the substrate to an electron acceptor, such as NAD<sup>+</sup> or FAD. Therefore they are redox enzymes since removal of hydrogen atoms is the equivalent to removal of electrons. The name is applied to both oxidation and reduction reactions.



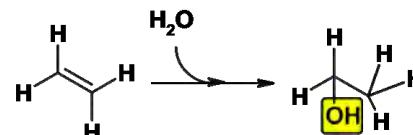
*Succinate dehydrogenase, an example from the citric acid (TCA) cycle, is shown. FAD is the obligatory co-substrate, accepting electrons in this case. Note that this enzyme could also have been called fumarate dehydrogenase.*

**Isomerase.** This class of enzymes rearrange functional groups on their substrates, releasing a product that has the same number of atoms as the substrate, but is an isomer of the original substrate. Unfortunately, the descriptive word "isomerase" is often omitted from their name.



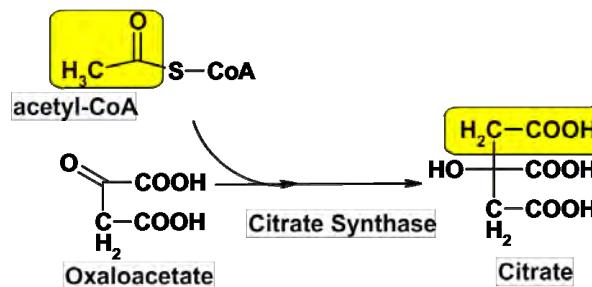
Aconitase is an isomerase that functions in the citric acid cycle to convert citrate to isocitrate. Note that the composition of both substrate and product are the same, but the chemical structure is not.

**Hydratase.** This reaction type, which has a number of idiosyncratic names in different pathways, adds water to a double bond.



The addition of water to a double bond to produce an alcohol.

**Synthetase.** These enzymes are responsible for the synthesis of more complex molecules from simpler substrates. For example, ATP synthase generates ATP from ADP and inorganic phosphate, a process that is driven by a proton gradient across a membrane. Citrate synthase catalyzes the following reaction, which is the first in the citric acid (TCA) cycle.



Citrate synthase combines acetyl-CoA and oxaloacetate to form citrate. The source of energy in this case is the high energy thio-ester in acetyl-CoA.



## Enzyme Nomenclature

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# Enzyme Nomenclature

## Question 1

The name of most enzymes consists of two words. The first word usually refers to the \_\_\_\_\_, while the second word refers to the \_\_\_\_\_ and has the suffix \_\_\_\_\_.

Select one answer.

- A. product, reaction type, "ase"
- B. substrate, reaction type, "ase".
- C. reaction type, substrate, "ase".

## Question 2

If an enzyme forms a bond between X and Y to form the compound Z, it is most likely to be a

Select one answer.

- A. dehydrogenase
- B. hydratase
- C. kinase
- D. synthetase

## Question 3

The reaction shown below is catalyzed by which enzyme?

Select one answer.

- ?
- A. PEP phosphatase
  - B. Pyruvate kinase
  - C. PEP kinase
  - D. Pyruvate phosphatase

## Question 4

If an enzyme is a dehydrogenase, it catalyzes a \_\_\_\_\_ reaction, involving \_\_\_\_\_, and/or \_\_\_\_\_.

Select one answer.

- A. phosphate addition, ATP, ADP

- B.** redox, NAD+, FAD
- C.** redox, ATP, ADP
- D.** phosphate removal, ATP, ADP

## Question 5

When comparing a kinase to a phosphatase, which of the following is true?

Select one answer.

- A.** None of these choices, as both names describe the same activity.
- B.** A kinase utilizes ATP as a source of phosphate.
- C.** A phosphatase produces ADP and inorganic phosphate.
- D.** A phosphatase is the reverse reaction of a kinase.

Check your answers

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# Proliferation (new for CC-OLI)

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## Learning Objectives

- Describe physiological events that would lead to cellular proliferation. List the steps of mitosis and cytokinesis and identify key cellular features related to the steps of proliferation.

When cells divide, they take a specific length of time to undergo the cell cycle. Therefore a group of cells will tend to replicate in concert. And due to each cell giving rise to another, the increase in cell number is exponential and the population doubles with each cycle (since 1 à 2 à 4 à 8 à 16...). This results in rapid growth, or proliferation, of the cell population. During development, as a fertilized egg develops into an embryo, and as its constituent cells differentiate and develop into various tissues, such proliferation is normal and necessary. However, in the adult body, cell proliferation is usually undesirable. With the slowing of development many cells are supposed to remain in the quiescent (non-growth) phase of the cell cycle. However, due to mutations, a cell may shift out of quiescence and begin to divide uncontrollably. With proliferation, the cell will form a tumor, and may result in a life-threatening cancer.

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 Apoptosis (new for CC-OLI) 

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# Apoptosis (new for CC-OLI)

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## Learning Objectives

- Define apoptosis and necrosis and describe the cellular processes associated with each.  
Provide examples of where apoptosis and necrosis occur in physiology.

How does a single fertilized cell develop into something as marvelous and intricate as the human body? Part of the answer is apoptosis or programmed cell death. For example, the early hand of an embryo is a stubby appendage. As cells between the fingers selectively die off, they sculpt the hand, leaving behind the separate fingers. In the adult apoptosis is one way that tissues maintain their integrity. Cells selectively die off to allow renewal of tissues such as stomach, lungs, liver and so on. If apoptosis ceases in the tissue's cells, a tumor can form, perhaps becoming cancerous. Apoptosis is distinguished from necrosis, which is cell death as a result of injury. Whereas apoptosis is internally determined, external trauma, toxins or infection cause necrosis. These different causes give rise to various classes of necrosis.

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# Module 3

## Tissues

### Learning Objectives

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- Define tissue. List the four major tissue types and organ systems associated with each.

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# Tissues (new for CC-OLI)

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## Learning Objectives

- Define tissue. List the four major tissue types and organ systems associated with each.

### Tissue

DEFINITION

A **tissue** is a group of cells with similar shape and function.

Consider how the body is organized. Tissues occupy a place between cells and organs. That is, a tissue is a group of cells with similar shape and function. In turn, organs (which comprise the body) are comprised of various tissues.

The component cells of tissue are a specific cell type. A tissue's cells may be identical, but not necessarily so. Several tissues will comprise an organ. For example, the contractile cells of skeletal muscle are bundled together to make muscle fiber tissue. In turn, endomysium cells form enclosing tissue that wraps around bundles of muscle fibers, like a tortilla around a burrito. Several of these structures are in turn wrapped by another tissue, perimysium. Finally, bundles of these are surrounded by a sheath of yet another tissue, epimysium, which covers the outside of the whole muscle. Yet more tissue is necessary for the muscle to function in the body. Connective tissue comprising ligaments attaches the muscle to the skeleton, and nerve tissue conducts impulses from the nervous system to signal the muscle to contract.

Skeletal muscle is only one kind of tissue. The body comprises dozens of different tissues, but broadly speaking they belong in one of four types.

- Muscle tissue (in turn divided into skeletal, smooth and cardiac) is contractile. It allows locomotion of the body. It also allows necessary contractions of various organs such as the heart, and respiratory and digestive systems.
- Nerve tissue comprises the body's wiring system. It conducts signals to or from the nervous system to various organs.
- Connective tissue holds the body together. It is found in most organs, anchoring them to the skeleton and other organs. Types of connective tissue include fibrous tissue, fatty tissue, loose tissue and cartilage. Connective tissue also includes bone, blood and lymph.
- Epithelial tissue is the body's protection against the outside environment. Skin tissue helps to maintain homeostasis. It helps monitor and control temperature, and resists abrasion, foreign bodies and damaging chemicals. Internally, epithelial tissue lines most internal cavities, secreting or absorbing nutrients.

Tissues form during development. Stem cells in the embryo differentiate into various cell types. The necessary genes in the cells turn on or off, resulting in the production of proteins that characterize a cell's structure and function. Early in embryonic growth, the cells migrate to the appropriate location in the body. Once there, they proliferate so that the tissue can perform its needed function.

Different tissues arise from the source cells in each of the three primary germ cell layers. For

example, the epithelium is derived from the ectoderm and endoderm. Connective tissue arises largely from the mesoderm. Gastrointestinal and respiratory tissues arise mostly from endoderm. Programmed cell death, or apoptosis, may take place to eliminate transitory tissues in the embryo, such as the pronephros, a simple excretory organ that is later replaced by the kidney.

## Learning Activities

What types of tissues are in your hand?

epithelial

connective

muscle

nervous

*all of the above*

clue: move your hand and think about all of the complex parts to it

if guessed anything but all of the above, the hand contains all of the above; we will help you identify them in the next exercise

Match the part of the hand with the tissue type (I'd like to have a longer list of parts than tissue types so students know it's not just 1 for 1)

epithelial - the skin that covers it

connective - the bones in the fingers, cartilage in the joints, blood in the blood vessels

muscle - the abductor pollicis brevis muscle

nervous - the sensory nerves for the sense of touch, the nerves that control the muscles

clue: epithelial tissue cover, connective tissue gives structural support, muscle tissue generates force, nervous tissue relays information

How does connective tissue provide structure and support?

the cells are strong

*structural fibers and dense extracellular matrix*

it doesn't

force generation

if guessed cells: some cells are stronger than others, but not enough to provide support to a whole organism

if guessed it doesn't: structure and support are hallmarks of connective tissue; blood is a connective tissue which doesn't seem to be very stiff but the large fluid content is very mechanically relevant

if guessed force generation: no, sorry. that's muscle tissue.

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# Module 4

## Organs

### Learning Objectives

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- Define organ. Discuss within the larger hierarchy of human physiology.

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# Organ (new for CC-OLI)

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## Learning Objectives

- Define organ. Discuss within the larger hierarchy of human physiology.

The **organ** level of organization in the body may be one of the most familiar to us from our everyday experiences. Many of the common ailments we hear about—an upset stomach, a broken bone, lung disease, skin cancer—are named for the organs they affect.

An organ is made up of tissues that work together to perform a specific function for the body as a whole. Groups of organs that perform related functions are organized into organ systems, which perform more general functions. The table below describes the structures and functions of some common organs.

Organ	Primary function (s)	Tissues it contains	Organ system(s) it is a part of
brain	control of body systems and behavior; cognition	nervous, connective, epithelial	nervous system; endocrine system
skin	protection; support and containment; temperature and fluid regulation	epithelial, nervous, connective	integumentary system
stomach	chemical and mechanical digestion of food	epithelial, connective, muscular, nervous	digestive system
sternum (breastbone)	support; protection; blood cell production	epithelial, connective	skeletal system; immune system; cardiovascular system
kidney	waste removal; fluid regulation	epithelial, connective	urinary system

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 Tissues 

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# Module 5

## Tissues

### Learning Objectives

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- Define organ system. Compare with motivation section and discuss within the larger hierarchy of human physiology.

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# Organ Systems (new for CC-OLI)

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## Learning Objectives

- Define organ system. Compare with motivation section and discuss within the larger hierarchy of human physiology.

Organ system	Key organ (s)	Primary function (s)
integumentary	skin	support; protection; regulation of fluid levels and temperature
skeletal	bones, cartilage	support; protection; movement; blood cell production
muscular	muscles, tendons	support; movement
urinary	kidneys, bladder, urethra	waste removal; regulation of fluid levels
digestive	tongue, esophagus, stomach, small intestine, large intestine, gallbladder, rectum	digestion of food; waste removal
respiratory	trachea, lungs	gas exchange; regulation of temperature
cardiovascular	heart, blood vessels	transport of materials through the body; regulation of temperature
nervous	brain, spinal cord	control of behavior and body systems; cognition
endocrine	glands	control of body systems and development
immune	thymus, tonsils, spleen	defense against infection
lymphatic	lymph nodes, lymphatic vessels	immunity; regulating fluid balance
reproductive	penis, testes, prostate (males); uterus, ovaries, vagina (females)	reproduction

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# Module 6

## The Whole Body

### Learning Objectives

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- Discuss how organ systems work together to maintain homeostasis within the body.

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# Whole Body (new for CC-OLI)

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## Learning Objectives

- Discuss how organ systems work together to maintain homeostasis within the body.

The whole body is...

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# Module 7

## Populations

### Learning Objectives

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- Discuss how the environment impacts physiology. Synthesize environmental factors which could impact homeostasis.

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# Populations (new for CC-OLI)

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## Learning Objectives

- Discuss how the environment impacts physiology. Synthesize environmental factors which could impact homeostasis.

Text about populations goes here.

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